JOURNAL OF

# The American Geriatrics Society

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THE JOURNAL OF

# The American Geriatrics Society

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## CONCERNING CEREBRAL ARTERIOSCLEROSIS

MILLER FISHER, M.D.*

*The Montreal General Hospital and Queen Mary Veterans' Hospital, Montreal, Canada*

There is a widespread tendency to attribute, unjustifiably, many neurologic disturbances to "cerebral arteriosclerosis" and it is the correction of some of these false ideas which is the aim of the present paper. Possibly the chief offense lies in the realm of senility. In this realm the physiologic and pathologic mental changes of the elderly are often dismissed as manifestations of vascular changes, the clinician having a very indistinct mental image of the actual neuropathologic lesions or events believed to be responsible. Epilepsy and fainting spells are all too readily laid at the door of arteriosclerosis, without pathologic proof. Dizziness, attacks of "vasospasm," disturbances of gait and balance, headache, mental depression and even sleeplessness are often attributed to hardening of the cerebral arteries, although diagnostic guide-posts for the clinician are for the most part still lacking. Arteriosclerotic Parkinsonism has remained a disputed clinical and pathologic entity in need of clarification. Another phenomenon attributed to arteriosclerosis is the unusual sensitivity of elderly people to drugs.

During the past three and one half years a methodical attempt has been made at The Montreal General Hospital and The Queen Mary Veterans' Hospital to examine in the pathology laboratory all the brains removed at autopsy, whether the history indicated cerebral disease or not. All readily available clinical data were checked before examination of the brain and later, if necessary, patients' files at other hospitals were examined; in special cases, histories were obtained in retrospect from the family of the deceased, in order to settle a particular point if possible. All specimens, a total of some 1,500, were examined by the author. For most of the clinical data, the writer is greatly indebted to the consultants and house-staff of all services, but in many cases the clinical details too, were personally obtained.

The term "arteriosclerosis" has a broad connotation and is used to refer to several types of sclerotic arterial disease. In this discussion of "cerebral arteriosclerosis" it is first necessary to define the subject as clearly as possible. At the

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* Lecturer in Neurology, McGill University, Montreal.

1952 meeting of the American Society for the Study of Arteriosclerosis an excellent classification of the arteriopathies was suggested (1):

1. *Degenerative arteriopathies:* atherosclerosis; medial arteriosclerosis; arterionecrosis (idiopathic, cystic medionecrosis of Erdheim and toxic).
2. *Productive and/or hyperplastic arteriopathies:* intimal and/or medial changes often associated with high blood pressure.
3. *Inflammatory arteriopathies:* arteritis due to infection, allergy, chemical or physical agent, or trauma; thromboangiitis obliterans.
4. *Combined forms of arteriopathies.*

In this list the only type of arterial disease which is of major importance in the production of cerebral symptoms and lesions is atherosclerosis, which term refers strictly to the process in which lipid accumulates beneath the intima. It is this arch-villain, atherosclerosis, which will be discussed herein and it is recommended that the term atherosclerosis always be used when referring to this particular vascular change. To avoid ambiguity and clarify terminology the term cerebral arteriosclerosis should be discarded and the specific pathologic diagnosis used whenever possible.

Before leaving this matter, a few remarks concerning the other arteriopathies may be in order. Mönckeberg's medial arteriosclerosis affects the larger arteries at the base of the brain but, as elsewhere in the body, it cannot be incriminated in the production of cerebral pathologic lesions. Erdheim's medial necrosis has not been described intracranially and I have not encountered it there. The thickening of the vascular wall associated with hypertension involves the media and/or intima and extends from the largest to the smallest arterial channels. The medial thickening (muscle hypertrophy) probably does not lead to functional narrowing of the lumen, since the increased head of pressure seems to maintain a normal blood flow. At any rate, no pathologic changes or clinical signs can be atrributed to a change only in the media. The nature of the intimal thickening of small arteries seen in association with hypertension is poorly understood, particularly its relationship to atherosclerosis of the larger vessels. The question arises as to whether or not the accumulation within the intima is merely the same lipid as in atherosclerosis, the difference in appearance being due to the vast difference in the caliber of the affected vessels. As will be discussed later, it is likely that ordinary easily-recognizable atherosclerosis of the smaller vessels (200–300 $\mu$ external diameter) is responsible for the lesions of hypertension, rather than other subintimal changes such as hyalinization or "onion-skinning" of the cerebral arterioles. Anders and Eicke (2) described "hyalinosis" of the medium and small cerebral arteries. This change was found in all of 34 patients with high blood pressure and in none of the normotensive controls. It was distributed in circumscribed fashion, not uniformly, and the authors found no relation to arteriosclerosis, although the hyalinized tissue stained readily for fat. "Hyalinosis" seemed related to hemorrhage rather than to softenings.

"Arteritis", other than those types associated with syphilitic or tuberculous meningitis, is rarely the cause of cerebral symptoms, the cerebral arteries usually being spared in polyarteritis nodosa, lupus erythematosis and in "temporal arteritis" (retinal artery excepted). The condition of "widespread intimal pro-

liferation of arteries with resulting thrombosis" recently reviewed along with the report of a new case by Whiteley and Wilson (3) has not been described in cerebral vessels. In regard to cerebral thromboangiitis obliterans, there is still disagreement as to whether it constitutes a distinct and specific entity. The characteristic pathologic picture in cases so diagnosed has usually consisted of a cerebral softening, the artery or arteries to which are whitish, opaque and occluded by a fine meshwork of connective tissue, presumably due to organized clot. Evidence of an arteritis is mild and may be due to adjacent brain infarction. Lindenburg (4), who described 22 cases, pointed out that thrombosis and embolism each can produce the same picture. The highest incidence of the disease was noted in persons over the age of 50 and there was often little evidence of similar disease in the limbs, both of these features being at variance with the usual view of Buerger's disease. The chief difficulty in interpreting cerebral thromboangiitis obliterans stems from the lack of clarity concerning the exact pathologic picture required for its diagnosis elsewhere in the body. Buerger's (5) concept arose from a study of limbs amputated because of gangrene and, as he appreciated, the role played by disease of the more proximal arteries of the lower limb could not be assessed. In this respect Lindbom (6), in his excellent pathologic and radiologic study of some 350 lower limbs, did not encounter the changes of Buerger's disease and suggested that a defect in blood coagulation should be suspected, rather than primary arterial disease. It will be recalled that in Buerger's cases the arteritis was not pronounced and was not maximal at the site of fresh thrombosis. In my opinion occlusion of the internal carotid artery or its branches and cerebral embolism are usually responsible for the picture of what is called cerebral thromboangiitis obliterans, the basic pathologic process being atherosclerosis in the former.

Having briefly referred to non-atherosclerotic vascular processes, discussion of atherosclerosis itself can be conveniently divided as follows: 1) the properties of atherosclerosis of cerebral arteries, 2) the pathogenesis of cerebral symptoms and lesions, and 3) the relation of various clinical phenomena to atherosclerosis.

## 1. PROPERTIES OF ATHEROSCLEROSIS OF THE CEREBRAL ARTERIES

The basic lesion is the same in the cerebral vessels as in similarly-sized vessels elsewhere in the body. The earliest recognizable lesion consists of a localized or focal concentration of lipid material (cholesterol, cholesterol esters, fatty acids) immediately beneath the endothelial lining. The fundamental cause of such a focal "deposit" is of course as yet unknown and equally obscure is the reason for the gradual enlargement of such a plaque until blood flow is significantly obstructed and the nourishment of cerebral tissue jeopardized. It is not known if the primary fault lies within the vessel wall or in the chemical content of the circulating blood, or in both. Atherosclerosis is not a function of age only, for some persons of 80 or 90 have the vessels of a youth.

The amount or degree of atherosclerosis in the cerebral arteries roughly parallels its severity elsewhere in the body. Occasionally the cerebral vessels will show much more than the abdominal aorta or the coronary and leg vessels, but this is not the rule and it is incorrect to emphasize that such a discrepancy can occur.

In the great majority of cases atherosclerosis shows a fairly uniform severity in various parts of the body. The coronary arteries unfortunately are rather small and their collateral circulation not reliable, so that atherosclerotic deposit all too frequently announces itself by its serious effects on the myocardium. Yet at necropsy vessels elsewhere will usually prove to be similarly involved. It might be added here that palpation of the radial artery is useless in assessing atherosclerosis or any other vascular disease in the remainder of the body. It has been known (7) for fifty years or more that the radial artery for some reason escapes the changes of other vessels, yet many clinicians still record "the feel" of the wall as a significant finding.

Atherosclerosis is primarily a focal disease and in early cerebral atherosclerosis the plaques are often strikingly localized to bifurcations, branchings and curves of the larger vessels at the base of the brain. In dealing with the cerebral circulation it is necessary to include all channels between the heart and the most peripheral cerebral twigs, for occlusion of the common carotid, internal carotid or vertebral arteries in the neck can as well impede blood flow, as can obstruction in their intracranial extensions. In this broader view of the cerebral circulation atherosclerosis is most prone to occur within the carotid sinus at the origin of the internal carotid artery, but other sites on both the basilar and carotid systems do not fall far behind. The special sites of predilection are as follows: the carotid sinus, the carotid siphon or paraclinoid portion of the internal carotid artery near the origin of the ophthalmic artery, the middle cerebral artery at its origin and at its first bifurcation, the vertebral arteries as they enter the craniospinal space at the atlas vertebra, the lower extremitity of the basilar artery, (union of vertebrals), the region of the bifurcation of the basilar artery, the posterior cerebral artery as it winds posteriorly around the cerebral peduncle and finally the anterior cerebral artery as it curves upwards around the genu of the corpus callosum (Fig. 1). This distribution well illustrates the influence of bifurcations, branchings and curves. For the most part it is these regions which must be considered when contemplating the possible sites of atherosclerotic obstruction or of superimposed thrombosis along the large vessels at the base of the brain. In more advanced atherosclerosis, intervening stretches of the arteries become affected but as a rule such deposits do not reach important dimensions. Significant atherosclerosis of the vertebral arteries in the neck has not yet been encountered but no doubt a rare case should occur. On the other hand occlusion of the cervical portion of the carotid system is not uncommon. The carotid and basilar systems are approximately equally affected.

Atherosclerosis in normotensive individuals tends to spare two important groups of smaller vessels: 1) the surface branches of the cerebrum and cerebellum, and 2) the penetrating branches to the lenticular nucleus and the internal capsule arising from the stem of the middle cerebral artery and to the thalamus and brain stem from the basilar system. In hypertension on the contrary, these two groups are particularly liable to be affected (Fig. 1) and when plaques can be seen in the surface vessels over the cerebrum or cerebellum, one can safely predict the presence of hypertension on the basis of this finding alone. Plaques along the surface vessels over the cerebrum are not often of clinical significance, and

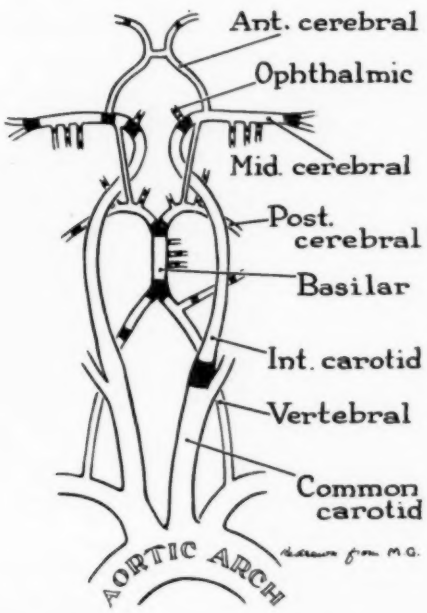


FIG. 1. Diagram of the cerebral arteries, showing the sites of predilection for atherosclerotic deposition. The smaller beaded vessels show the localization in the presence of hypertension, these vessels not being affected in normotensive subjects.

involvement of the surface cerebellar arteries only infrequently leads to infarction. Of special importance are the plaques in the penetrating branches, as they constitute one of the commonest causes of focal brain softening. This difference in the behavior of the surface and the deep vessels lies in the fact that the former have a good anastomosis with neighboring vessels, whereas the penetrating branches to the lenticular nucleus, internal capsule and brain stem are functionally end-arteries, obstruction being therefore poorly tolerated. The external diameter of the smallest vessels in which atherosclerosis is seen is in the neighborhood of 200 $\mu$—occasionally 100 $\mu$. Thus one would not expect to find atherosclerosis in the branches of the central retinal artery, bearing out the clinical impression that ophthalmoscopic examination is of no use in assessing atherosclerosis, either in the large cerebral arteries or elsewhere. Each of the cerebellar arteries is of such a size that atherosclerotic occlusion is practically always associated with hypertension.

Hypertension, in addition to "pushing" atherosclerosis out into the two groups of smaller vessels just mentioned, aggravates the deposit in the larger vessels so that occlusion is still liable to occur in the large arteries at the base. Hypertension, moreover, alters the distribution of atherosclerosis so that instead of the focal intimal deposit of the normotensive vessel a more uniform layer or coat is laid down, producing yellow or white tubes with a superficial "tree-barking" appearance. It is possible, from finding this uniform coat of atherosclerosis along the basilar artery at autopsy, to predict safely that hypertension had been present.

Atheromatous (this term is used for any stage of the atherosclerotic process)

deposits are unusually easy to see in cerebral vessels because of the thinness of the wall and the absence of surrounding fat or connective tissue. The cerebral arteries are unique in this respect, for without opening up or sectioning the vessel the slightest abnormality can as a rule be seen, even in channels no larger than 200 $\mu$. It is thus possible to observe great variation in the color of the atherosclerotic plaques. In some cases the deposits are gray or pale cream in color, whereas in others they are strikingly yellow or even yellowish-orange. The former usually means a more benign disease, whereas yellow atherosclerosis indicates a more acute or malignant stage. With great regularity one can suspect from finding yellow plaques on superficial examination that not only will softenings be found within the brain but also that the patient had had serious vascular disease elsewhere, probably succumbing to myocardial infarction. Hemorrhage into plaques of intracranial atherosclerosis is not uncommon and is found chiefly in the most aggravated form when the bright orange staining of hematoidin can be seen at the affected site. Hemorrhages into atherosclerotic deposits within the carotid sinus are particularly common.

A few minor points remain. It should be remembered that the cerebral arteries, in addition to atherosclerotic deposition, show the changes of age and of wear and tear. These changes are difficult to define but readily seen. In the young, the cerebral vessels are small and almost transparent. With increasing age a highly variable degree of enlargement, thickening, opaqueness and redundancy appears, so that apart from lipid deposit, one aged person may have tiny, thin-walled vessels whose capacity to carry sufficient blood would be questioned, whereas another displays the huge tortuous "pipe-stems" frequently pictured in pathology texts. In my experience great enlargement and tortuosity are usually associated with hypertension, but not all cases of hypertension show such a change. Obviously it will take a thicker or larger deposit of atherosclerosis to occlude the lumen of an enlarged artery, dilatation having in this respect a beneficial effect. Atherosclerosis tends to be deposited in the bulging wall of berry-aneurysms, probably being secondary rather than primary. From a theoretical point of view, such deposition provides an opportunity to study the behavior of atherosclerosis in the absence of elastica and media. It is my experience that atherosclerosis plays no part in the genesis of berry-aneurysm. "Arteriosclerotic aneurysms" usually consist of extreme redundancy and fusiform ballooning of an atherosclerotic basilar, vertebral or internal carotid artery in the presence of high blood pressure. They are rare and usually but not always asymptomatic. Vascular syphilis, too, can lead to local ballooning of the basilar artery.

In summary, atherosclerosis is a focal disease and certain sites show a predilection to development of plaques. It is these sites which must be kept in mind when considering the effects of atherosclerosis. Hypertension leads to deposits in the smaller penetrating and surface vessels and, in addition, tends to produce a more uniform layer in the larger arteries. Cerebral atherosclerosis, in general, parallels the process elsewhere in the body. The different colors of the plaques are indicators of the malignancy of the process. The cerebral vessels are ideal for studying the atherosclerotic process.

## 2. PATHOGENESIS OF CEREBRAL SYMPTOMS AND LESIONS

Next to be considered is the manner in which atherosclerosis elicits its harmful effects. In most instances simple mechanical obstruction of the blood flow seems to be responsible. This obstruction can be due directly to the intimal plaque bulging into the lumen or, as is more often the case, it follows superimposed thrombosis. Total occlusion does not result from an atherosclerotic plaque alone, a small eccentrically-placed channel usually persisting until thrombosis occurs. It is probably a reliable rule that cerebral thrombosis *in situ* is always preceded by atherosclerosis, except for the uncommon case of arteritis or other rare arteriopathy. To signify this association of atheroma and thrombosis and provide a name for easy reference, the term *atherothrombosis* is suggested. Regarding other ways in which atherosclerosis may lead to trouble, it might be mentioned that there is a widespread but by no means unanimous impression that atherosclerotic vessels can become occluded temporarily by "vasospasm." Also atheroma within the carotid sinus has been held to set off widespread cerebral vasospasm (8). Finally atherosclerosis of the arch of the aorta, common carotid artery or carotid sinus can ulcerate, with the formation of mural thrombus, pieces of which may act as cerebral emboli. One often hears of cerebral hemorrhage attributed to rupture of a plaque of arteriosclerosis but such an event has never been confirmed personally. Atherosclerosis probably plays no important part in primary intracerebral hemorrhage.

The results of atherosclerotic impediment to the cerebral flow are not always easy to estimate. For example, I have found complete blockage of one internal carotid artery in the neck in several cases in which no symptoms had been present during life and the brain showed no pathologic alterations at autopsy. It is well known that surgical ligation of one carotid artery can be carried out in many cases without harm. Similar obstruction without any known symptoms has been found in the middle cerebral, posterior cerebral, anterior cerebral, vertebral and posterior inferior cerebellar arteries. In the case of the internal carotid artery, compensatory blood flow probably comes via the ophthalmic artery and the circle of Willis. In the case of the vertebral artery, the opposite vessel can carry sufficient blood, provided it is not congenitally small. Innocuous obstruction of the other arteries mentioned must mean that adequate collateral blood flow from adjacent arteries can reach the entire territory of each of the major cerebral arteries. Such striking findings, along with the fact that it is extremely common to find vessels narrowed to the point of virtual occlusion without any symptoms whatsoever, suggest caution in too readily attributing symptoms to the effect of nonoccluding or even occluding atheromatous plaques.

An important factor in determining the result of obstruction of a cerebral vessel is the speed with which the final occlusion occurs. In embolism, in which instance blockage probably occurs rapidly (an assumption), the infarct or softening as a rule conforms rather accurately to the classic territory of the occluded artery. In thrombosis, the size of the infarct is highly variable, ranging from none at all as described previously, through a small area of softening adjacent to the site of obstruction, to infarction of almost the entire territory, mimicking

embolism. The more gradual the final occlusion the more chance there is for adequate collateral flow to become established. The resultant infarct will also be determined by the availability of pre-existing collateral channels and by the level of the systemic blood pressure.

The relative importance of these various factors is difficult to assess, because of our limited knowledge of the chain of events leading to thrombosis. As already stated, cerebral plaques by themselves probably never lead to complete obstruction of the lumen, superimposed thrombosis usually being necessary to produce occlusion. In the production of the final thrombotic occlusion of the lumen, great importance is attached to subintimal capillary hemorrhage (*i.e.*, into the plaque) by Paterson (9) in the case of coronary and cerebral vessels and by Lindbom (6) in the case of the leg arteries. Horn and Finklestein (10) attribute coronary thrombosis to such mural hemorrhages in 62.5 per cent of cases. Both Paterson and Lindbom suggest that bleeding into the plaque alters the overlying endothelium, leading to thrombus formation, whereas Horn and Finklestein suggest, in addition, that hemorrhage into a plaque can produce sufficient enlargement to block the lumen directly. The rate of extravasation of blood in mural hemorrhages is not known. In my cases it has not been uncommon to find abundant hematoidin pigment in the vicinity of a vascular occlusion, indicating that hemorrhage into a plaque played a part in precipitating closure of the vessel. Incidental mural hemorrhage is deemed to be as common in cerebral arteries as in the coronary and leg arteries (6, 9).

Cerebral atheromas do not ulcerate, at least grossly, to provide a nidus for clotting; and mural thrombus which might indicate microscopic ulceration is not evident upon routine examination. Usually extreme narrowing of the lumen takes place before thrombosis occurs, suggesting that physical factors play a part either by damaging the surface of the plaque or altering the stability of the blood so that clotting is enhanced. Some authors have found an increased coagulability of the blood in atherothrombosis but Kadish (11) was unable to confirm this. There is need for further detailed pathologic study of the sites of cerebral thrombosis, in an effort to assess the importance of all the various factors. The cerebral vessels are especially well suited to such an investigation, for the vessels are easily examined and their territories well known. Furthermore, cerebral tissue is extremely sensitive to ischemia, easily recognizable symptoms or signs are liable to appear with the mildest provocation and finally the oxygen requirements of the brain are almost constant in contrast to the myocardium.

Thus, at the present time, there are no accurate ideas as to the speed with which the finally-occluding thrombus can develop or usually develops. As has been pointed out elsewhere (12), straightforward cerebral thrombosis is often associated clinically with temporary warning symptoms prior to the onset of a major stroke and this could mean that building up of the thrombus is an intermittent process, although there are alternative possibilities, including such occurrences as vasospasm, the failure of collateral flow, a fall in systemic pressure, or intermittent hemorrhagic extravasation into the plaque. Although the onset of the stroke in cerebral thrombosis is usually a stuttering one, fragments of paralysis

being added over a period of hours, days or weeks, in some cases the onset is abrupt, suggesting that final occlusion by the growing clot is sudden. In this regard one might speculate that the main bulk of the thrombus as it enlarges could shift distally a short distance from a position just proximal to the greatest narrowing and thus plug the remaining lumen suddenly. Paterson (9), by serial section, found the oldest part of the occluding thrombus to lie proximal to the point of greatest stenosis, thus favoring such a possibility. However, Horn and Finklestein (10) concluded from their studies that the oldest part of the thrombus lay at the point of greatest narrowing, not proximal to it. Of course, a sudden onset of symptoms without prodrome could result from hemorrhage into a plaque, with immediate blockage of the lumen. Theoretically it should be impossible for capillary bleeding to reach proportions sufficient to block the lumen in the face of full arterial pressure, but Horn and Finklestein found such a state of affairs in 13 cases of coronary occlusion.

It is possible that during the process of thrombus formation pieces of clot become detached and are carried further peripherally as emboli. Fresh cerebral emboli have been encountered distal to an old carotid occlusion, indicating that the two processes are not mutually exclusive by any means. It must be remembered that ordinary cerebral emboli originating in the heart can become arrested at a narrowing due to atherosclerosis, giving the false appearance of thrombosis. This is probably a common occurrence and at times there is no way of distinguishing such emboli from thrombosis.

Whatever the details of the occlusive process may be, atherosclerosis causes symptoms and lesions in the great majority of cases by leading to thrombosis. The foregoing discussion is applicable not only to involvement of the large vessels at the base of the brain but also in a large part to the small penetrating vessels running to the basal ganglia and brain stem, vessels which, as already stated, are largely spared in normotensive subjects, but are prone to involvement in the presence of hypertension. These small arteries pass to the deeper parts of the brain where tracts and functions are greatly concentrated and where a small lesion causes a disproportionately serious clinical picture. The softenings produced by blockage there, are only a few millimeters in diameter and in the healing stage produce the état lacunaire of Marie. There is an excellent correlation between these lesions and the presence of both hypertension and atherosclerosis, neither being sufficient in itself. The only exceptions to this rule are in occasional diabetics and in the extremely aged. These lacunes are the pathologic substrate of many of the minor strokes seen in hypertension, and of pseudobulbar palsy and mental deterioration. At present we use the term "hypertensive atherosclerotic encephalomalacia" for these lesions. In cerebral thrombosis associated with hypertension, the cerebral cortex is largely spared. Therefore, in thinking of the pathologic counterpart of hypertensive strokes, one must focus especially on the deeper structures, provided that cerebral embolism (which can well complicate hypertension) can be ruled out. While on the subject of hypertension, its apparently beneficial effect on collateral blood flow should be mentioned. Judging from pathologic observations, it would appear that when the

obstruction, be it atherosclerotic, thrombotic or even embolic, is in the larger vessels at the base of the brain or in the surface vessels, the presence of hypertension is an important factor in driving collateral blood to the involved territory across the circle of Willis and through surface anastomoses. This might be one explanation for the relative sparing of the cortex in hypertension. A similar action of hypertension probably operates in the case of occlusion of the coronary or lower limb vessels. From a theoretical viewpoint such an enhanced collateral flow would not be all gain, for the increased arteriolar tone associated with systemic hypertension, if still present, would have to be overcome.

Thus far the critical importance in the causation of symptoms of a fall of the systemic blood pressure has not been considered. The development of focal neurologic signs and symptoms during the hypotensive period, associated with massive gastrointestinal hemorrhage, myocardial infarction or overdosage of antihypertensive drugs, is well recognized. No doubt peculiarities of the anatomic pattern of the circle of Willis or its branches account for some of these, but ischemia distal to a partially occluding atherosclerotic plaque is a major cause. In our laboratory, the carotid vessels in the neck are being routinely examined at autopsy, and in several cases of acute circulatory collapse, the development of a hemiplegia could be shown to be determined by unsuspected almost total atherosclerotic obstruction of the internal carotid artery in the region of the carotid sinus. Blockage of other cerebral arteries by atheroma must operate in the same way. Indeed an old asymptomatic occlusion, such as mentioned at the beginning of this section, may be unmasked by a fall of blood pressure. The resultant cerebral symptoms may be transitory or persistent; in the latter case thrombosis or clotting may have occurred, or the period of ischemia may have been sufficiently long to have damaged the brain tissue irreversibly. Five cases have been examined so far in which one or both carotid arteries in the neck were found to be thrombosed over great lengths, following the development of a hemiplegia during a period of shock. Closely related to the question of hypotension is the special tendency for cerebral thrombosis to occur during sleep. The usual explanation for this is that during sleep the cerebral blood flow diminishes but Kety (13) has stated that in the only case in which he was able to make a study (only partially satisfactory) of the cerebral blood flow during sleep, there was a definite increase. It is difficult to fit such a finding into one's clinico-pathologic experience, which would rather suggest that clotting is enhanced during sleep, presumably due to decreased blood flow which also would at the same time tend to produce ischemia distal to an atherosclerotic plaque and diminish collateral blood flow.

One usually visualizes a thrombus as producing symptoms by blocking blood flow to the peripheral distribution of the involved vessel. On several occasions, however, I have found a total vascular occlusion of the middle or posterior cerebral artery with no softening in the corresponding peripheral portion but with infarction of deep structures due to blockage of the mouths of the penetrating arteries arising at the site of the thrombus. Such an event illustrates again how good the superficial collateral anastomotic blood flow can be, and secondly it demonstrates how a lacune can be produced in the basal ganglia in the absence

of hypertension and without atherosclerotic material being deposited in the penetrating branch.

A detailed consideration of the relation of atherosclerosis to vasospasm is beyond the scope of this paper. The chief evidence against the concept of vasospasm has been marshalled by Denny-Brown (14) and Pickering (15) but the question is far from settled. Only when clinical, pathologic and experimental human data are accurately known and analyzed should the suggestion of vasospasm be advanced, for alternative explanations are not lacking and all cases probably do not have a common mechanism. In the present state of our knowledge, it is advisable to look for an alternative mechanism and use the term vasospasm as sparingly as possible. In most cases which fall within the scope of cerebral vasospasm the transient symptoms and signs herald the onset of a more serious stroke, *i.e.*, the vasospastic phenomena are closely linked to the impending failure of a borderline circulation. In such cases atherosclerosis, along with superimposed thrombosis, is primarily responsible. Recently the beneficial action of anticoagulants in "vasospastic" episodes was reported (16) but the explanation for the cessation of the transient attacks is not evident. Several further cases have since been similarly treated with equally good results. It is unlikely that atheroma itself induces a local spasm in cerebral blood vessels, for were this so, most people over the age of 50 would be in the constant throes of attacks of all kinds. Paterson (9) postulated that hemorrhage into a plaque might lead to irritation and contraction of the adjacent muscle of the media.

The formation of a mural thrombus upon ulcerated atheroma needs scarcely to be mentioned. Such thrombi are not uncommon on the arch of the aorta and the large vessels arising therefrom. In addition, the large plaques of atherosclerosis which form within the carotid sinus likewise ulcerate. Cerebral emboli arising from such deposits may be regarded as a complication of atherosclerosis, if we adopt the broader view of a cerebral circulation suggested earlier. It is most difficult to establish with any certainty that a cerebral embolus arose from a mural thrombus and usually the diagnosis is a tentative one made by exclusion.

In summary, atherosclerosis by itself does not cause symptoms unless hypotensive vascular collapse occurs. Moreover, total occlusion of various cerebral arteries has been found without having caused lesions and in the absence of symptoms. In the majority of cases symptoms are elicited only when thrombosis is superimposed and the blood supply to the corresponding cerebral tissue compromised. In essence, strokes are the chief counterpart of cerebral atherosclerosis. The development of thrombosis in relation to atherosclerosis is poorly understood. Cerebral vasospastic attacks can be linked to atherothrombosis in most instances but the mechanism by which they are prevented by anticoagulant therapy is still obscure.

### 3. THE CLINICAL PICTURE OF CEREBRAL ATHEROSCLEROSIS

As stated in the foregoing summary, atherosclerosis leads to neurologic disease, chiefly by causing strokes, but this is not the appropriate place to enter into a detailed discussion of the myriads of clinical pictures which may characterize

cerebrovascular accidents. Fortunately some degree of hemiparesis or hemiparesthesia is usually present to facilitate the diagnosis, but when mind, memory, speech, vision, balance or coordination are alone disturbed an accurate clinical appraisal is no easy matter. Rather than describing such strokes the purpose of this paper may be better served by considering the part played by atherosclerosis in the production of various complaints attributed to it, perhaps erroneously.

1. *Senile dementia.* The vast territory comprising the dementias of old age is still far from clearly mapped. Assuming that the various well-recognized causes of dementia (such as syphilis, trauma, subdural hematoma, primary and secondary tumor, alcohol, hypovitaminosis, demyelinating disease, metabolic disorders, and Huntington's chorea) have been excluded, there then remains the clinical problem of differentiating "idiopathic senile dementia" from "cerebral arteriosclerosis." Many cases with the most advanced degree of senile dementia show little or no atherosclerosis of the cerebral arteries. In other cases a severe degree of atherosclerosis is present and the question arises as to its contribution to the genesis of the dementia. The answer is made difficult owing to our lack of a complete neuropathologic delineation of *all* the senile dementias. It is not clear how many different types there may be and, since a classification on clinical grounds is not reliable, it is dangerous to conclude that atherosclerosis plays no part until it is established that the neuropathologic change is the same, whether atheroma is present or not.

The presence of senile plaques and Alzheimer's neurofibrillar change has been customarily regarded as sufficient to establish the diagnosis of "idiopathic senile dementia." However, Sjögren and associates (17) refer to 10 cases of dementia and cerebral atrophy, with neither senile plaques nor neurofibrillar change. Also Gellerstedt (18) was unable to correlate the presence of either of these changes with mental deterioration, finding them as frequently in cases of normal mentality. Thus these two pillars of neuropathologic diagnosis may prove not to be reliable guides. In view of such confusion, it is manifestly difficult to assign proper significance to any cerebral atherosclerosis. Since atherosclerosis is a focal disease, it follows that dementia resulting from it should be attributable to a focus or foci of cerebral disturbance. However, since the anatomic localization of the various cerebral functions which comprise the mind are unknown, the pathologist does not know where in the brain to search for any minor or circumscribed ischemic effects of atherosclerosis.

What has been said so far applies to cases of dementia in which no gross cerebral lesions other than atrophy can be found. In such cases at the present time I do not incriminate atherosclerosis of the cerebral vessels, no matter how severe, because in hundreds of cases with an equal severity of vascular change and no obvious difference in distribution, the mind has been well preserved. Certainly when senile plaques are found in abundance, any atherosclerosis present is judged to be incidental. In my experience "cerebral arteriosclerosis" is diagnosed much too often in cases of dementia. These are tentative conclusions only, but fit the facts up to the present time. There is possibly one exception, namely bilateral occlusion of the carotid artery in the neck. In the past few years 5 cases of senile

dementia have been encountered in which both internal carotid arteries were blocked by atherosclerosis and superimposed thrombus. In reporting the first of these (19), the suggestion was made that such unsuspected occlusion and the resultant cerebral ischemia might furnish an explanation for some of the dementias of old age. The possible significance of bilateral carotid occlusion and the resultant cerebral ischemia in the causation of dementia is still to be settled, but so far no case of bilateral occlusion with normal mentality has been found.

When gross cerebral lesions are found in a case of dementia it becomes still more difficult to lay down any rules. Only thrombotic lesions, because of their linkage to atherosclerosis, will be considered here, but obviously cerebral embolism and hemorrhage are capable of eliciting similar effects. Not infrequently cerebral lesions, single or multiple, prove to be compatible with a fairly normal mentality. Thus the old question arises again: where must a lesion be to cause dementia, or if site is less important than number and size, how abundant and how large must the scattered lesions be? In my experience, gross vascular lesions associated with dementia have been in the thalamus, the territory of the anterior cerebral artery or so situated as to evoke some aspect of dysphasia or agnosia. Atherosclerosis can cause dementia only by leading to cerebral thrombosis and resultant brain softening. Such softenings usually occur over a rather brief period and at the onset involve adjacent areas transiently. Thus dementia due to cerebral atherosclerosis should have a relatively sudden onset, in contrast to idiopathic senile dementia which begins insidiously. In addition to the details of onset, the possibility of mild long-tract signs at the onset must be sought for. On examination one must make sure that the patient's dementia is not part of an unapparent dysphasia. Often a hemianopsia will betray the presence of a focal lesion. The presence of hypertension and its known proclivity to produce multiple small cerebral lesions (lacunes) favors, but does not unequivocally indicate, the diagnosis of dementia due to gross cerebral changes, for hypertension by no means precludes the development of senile dementia. Usually by the time hypertension leads to dementia, some evidence of pseudobulbar palsy is at hand. The course of the dementia is of significance too, for senile dementia is of gradual progression, whereas a dementia due to a stroke should be stationary or even improve; if there is a relapse, it should be abrupt again. Finally it is possible that gross cerebral lesions and idiopathic senile dementia both be present; in such a case, either or both may be responsible for the mental change. It is usually regarded as a hopeless task to attempt to unravel the focal mental functions of the brain, using the lesions produced by cerebrovascular disease, but I do not share this view.

The possibility of widespread small-vessel disease leading to dementia is often suggested. Scholz (20) has described "drusige Entartung" of the cerebral arteries and capillaries in 12 per cent of people over 70, but apparently it did not parallel senile mental deterioration. Capillary fibrosis, *i.e.*, an increase of adventitial fibers around capillaries, seen by silver impregnation methods, could interfere with exchange of nutriments between blood and tissue; but Gellerstedt (18), finding it in 86 per cent of elderly people with normal mentality, regarded the change as a purely senile manifestation. The "hyalinosis" reported by Anders

and Eicke (2) was not studied from a clinical point of view, but it is unlikely that nonoccluding vascular disease of medium-sized vessels could cause parenchymal changes. Thus, there is no evidence that small-vessel disease produces dementia.

In summary, if the dementia is of slow onset, if the patient is normotensive and there is no suggestion of non-mental neurologic abnormalities (by history and examination), the diagnosis of senile dementia is entertained. If there has been a stroke or if the dementia has been of rather abrupt onset, dementia due to a gross cerebral lesion is suspected, particularly if dysphasia or a hemianopsia can be demonstrated and if the patient is hypertensive. Except for bilateral carotid occlusion, atherosclerotic narrowing of vessels is not regarded as a cause of dementia and "cerebral arteriosclerosis" elicits mental deterioration only in so far as it has caused strokes, perhaps not recognized as such because of lack of paralysis or sensory change. What has been said in the case of thrombotic softenings holds equally well for cerebral hemorrhage and embolism. The cause of idiopathic senile dementia must be sought in other spheres than anoxia or ischemia.

2. *Epilepsy.* Not uncommonly, seizures developing in later life are attributed to "cerebral arteriosclerosis." During the present study an effort was made to determine the frequency of such an occurrence, and in no case was this diagnosis justified. When seizures began in late life and vascular disease was responsible, a gross lesion, either infarction or hemorrhage, was found in the cortex or immediately adjacent to it. Thus, atherosclerosis in order to cause epilepsy must lead to a cerebral softening, presumably via thrombosis. In general, cerebral embolism of the "silent" type and small cerebral hemorrhages are much more frequently the cause of epilepsy than is atherothrombosis.

3. *Dizziness.* In accurately determining the rôle of atherosclerosis in the production of dizziness, the same difficulty is met with as in dementia, namely, our incomplete knowledge of all the pathologic or patho-physiologic substrates of dizziness. The inner ear and its vessels have not been examined in the present group of cases but, judging from the behavior of atherosclerosis in other cerebral vessels, it is unlikely that it will be found even in hypertensive subjects, within such small vessels as supply the labyrinth. When dizziness co-exists with deafness and tinnitus the diagnosis of Ménière's labyrinthopathy is favored and this does not parallel in any way the presence or severity of cerebral atherosclerosis. Dizziness, *i.e.*, a spinning or giddiness and not just a peculiar head sensation, can occur at the onset of an acute stroke but is uncommon. Its chief incidence in cerebrovascular disease is found in occlusion of the vertebral, basilar and posterior inferior cerebellar arteries; by the time the patient comes to autopsy, thrombosis and complete occlusion of the involved vessel are present. It is not widely appreciated that the onset of a stroke due to basilar or vertebral artery occlusion is often preceded by transient attacks of rather typical dizziness which, if heeded, may provide an opportunity to try anticoagulant therapy. I have viewed with suspicion the large plaques of atherosclerosis often present in the basilar system and also the huge sinuous vertebral and basilar arteries, but have not been able to establish any relationship with the complaint of dizziness. Thus in the present state of our knowledge, dizziness as an isolated complaint should not be attrib-

uted to "cerebral arteriosclerosis," except as it connotes impending atherothrombosis within the vertebral-basilar system. Whether or not hypertension can cause harmful vascular changes within the labyrinth is not known, but for the reasons previously indicated there is no need to make such a postulate. Audiometric studies rather than caloric tests, in a group of hypertensive patients might help to solve the problem.

4. *Arteriosclerotic Parkinsonism.* This appellation is used to refer to the development of muscular rigidity and a short-stepping gait in elderly arteriosclerotics. However both the pathologic substrate and the clinical picture are far from substantially established. Critchley's (21) authoritative paper, although chiefly clinical in scope, classified the pathologic changes into three types: 1) gross vascular changes (softenings, lacunes), 2) minute vascular lesions, and 3) changes consequent upon old age. Without knowing further details, the term "arteriosclerotic" is hardly justified on such evidence and, furthermore, cerebral embolism and small hemorrhage had not been ruled out. Actually, exact clinicopathologic studies are almost non-existent. Foerster (22), who first drew attention to the clinical condition, found macroscopic brain softening in some cases but not in the majority. He suspected damage to the cerebellar peduncles as the cause of the rigidity. Collins (23), in describing similar cases, said gross lesions were not to be found pathologically. Pierre Marie (24), in his classic description of *l'état lacunaire* referred to *marche à petit pas* as a sign, but he emphasized its relation to repeated attacks of mild hemiplegia rather than to Parkinsonism. Insofar as extensive lesions of the basal ganglia often fail to produce muscular rigidity, the co-existence of such lesions and extrapyramidal signs in any one case may be only coincidence.

In describing the clinical picture, most authors underline the vast array of associated signs and symptoms, rigidity often occupying a relatively minor position. For example, in Foerster's cases dementia was constantly present and bladder disturbances commonly so. Critchley classified his cases into five types, each representing various bits of the full-blown picture of pseudobulbar palsy (such as dysarthria, dysphasia, emotional lability, dementia, incontinence, or pyramidal signs). Rhythmic tremor is almost never present, so that the total picture is far from reminiscent of paralysis agitans (mind and bladder function preserved, no pyramidal signs). Apparently the onset can be either sudden or gradual and the course most unpredictable. The tendon reflexes may be exaggerated and a Babinski sign elicited, pointing to a pyramidal type of rigidity. In many cases a mild attack of hemiplegia has occurred and it is questionable if the rigidity present thereafter should be straightway attributed to an "extrapyramidal" lesion, simply because clear-cut "pyramidal" signs are missing. The affection as described is usually bilateral and symmetrical, something not to be expected from ischemic vascular lesions.

Although the exact extent of the pathologic lesions responsible for paralysis agitans is not known, it is possible that multiple cerebrovascular lesions may occasionally produce the same effect, atherosclerosis being thus incriminated insofar as it leads to thrombosis and infarction. However, in the case of muscle

rigidity associated with evanescent hemiplegia, small strokes, or fractions of pseudobulbar palsy, it is preferable to diagnose the basic pathologic process (atherothrombosis, hypertensive atherosclerotic encephalomalacia, embolism, or hemorrhage) rather than single out one particular sign and impute to it a close relationship to paralysis agitans. Uncomplicated atherosclerosis, *i.e.*, without thrombosis, will not produce the syndrome. From a theoretical point of view, the nature of the rigidity and its anatomic substrate, although still uncertain, could be important in helping to unravel the problem of Parkinsonism in general, but first more detailed clinico-pathologic studies are needed. It is likely that the rigidity of very elderly people and of the senile demented is not at all related to vascular disease.

5. *Headache.* Simple atherosclerotic plaques are not painful. It is not clear if hemorrhage alone into a plaque can lead to pain. However, when thrombosis is superimposed and especially when a stroke is imminent, headache is not infrequent. Pathologically confirmed occlusions of the internal carotid, middle cerebral, posterior cerebral, vertebral, basilar, posterior inferior cerebellar and superior cerebellar arteries have been encountered in association with headache. The site of the headache in the first 3 instances was over the ipsilateral eye; in the last 4, over the occiput, often lateralized. The large vessels at the base of the brain give rise to pain fibers but it is not evident how and why thrombosis causes pain, when simple atheromatous deformation of the wall does not. Headache should not be attributed to "cerebral arteriosclerosis" without more accurately picturing the actual pathologic process.

6. *Head noises.* Of all the minor facets of neurology, this is as obscure as any. Apart from typical tinnitus and a few cases due to arteriovenous aneurysm, there are no rules for the interpretation of head noises. Often the sound is synchronous with the pulse; in the present study several such cases have come to autopsy but, in most, no anatomic or other vascular basis could be found. One very interesting case concerned an elderly lady who complained of a pulsation in the right side of her head. During right-sided arteriography she lost consciousness for about a minute but could be revived. Following subsequent intracranial exploratory operation she failed to respond properly and was found to have a complete *right* hemiplegia with aphasia, *i.e.*, the hemiplegia was on the same side as the head-noise. At autopsy an old complete occlusion of the left internal carotid artery was found in the neck, the right-sided pulsation or bruit probably being due to an enhanced flow in the remaining carotid artery. Another similar case has been seen clinically.

7. *Miscellaneous.* In the opening paragraph of this paper several complaints were listed which are loosely attributed to "cerebral arteriosclerosis." Some of these, for example, sleeplessness, slowing-up, depression, or sensitivity of elderly patients to drugs, have no relation to atherosclerosis. Others, such as disorders of gait and balance are not to be attributed to atherosclerosis in the absence of a stroke or strong suspicion thereof, as judged from an accurate history and examination. Cerebral atrophy or cerebellar atrophy are often regarded as the result of "arteriosclerosis" but in most cases there is no relationship whatever.

The gradual diminution in vibratory sensitivity in the lower limbs has been attributed to spinal arteriosclerosis without any satisfactory proof and in all likelihood there is no connection, since spinal vessels only rarely display atheromatous deposits. Another field in which the term "cerebral arteriosclerosis" is used too loosely is electroencephalography, in which electrical abnormalities are often judged to be compatible or not with arteriosclerotic vessel disease. Again, it is to be emphasized that the pathologic process must be visualized in terms of a localized cerebral lesion or lesions and not of a vaguely defined scattering of atherosclerotic plaques.

SUMMARY

Starting with the premise that many clinical symptoms are too readily attributed to "cerebral arteriosclerosis", that form of arteriosclerosis more accurately known as atherosclerosis is described in regard to 1) its pathologic aspects and 2) the way symptoms and lesions are produced. Atherosclerosis usually does not lead to symptoms, without superimposed thrombosis. The pathologic correlates of atherosclerosis must be thought of in terms of infarcts, large and small. The problem of thrombosis and its relation to vascular collapse, sleep and vasospasm have been touched upon. Finally, the author's opinions concerning various clinical phenomena usually attributed to cerebral arteriosclerosis are presented.

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# THE CALCIUM TOLERANCE TEST IN SENILE OSTEOPOROSIS* †

HERTA SPENCER, M.D., AGNES HAUSINGER AND DANIEL LASZLO, M.D.

*The Division of Neoplastic Diseases, Montefiore Hospital, New York, N. Y.*

This presentation deals with senile osteoporosis. Its incidence appears to be much higher than reported in the literature, because most of the cases are relatively asymptomatic and, therefore, remain unrecognized. Anatomically osteoporosis is characterized by a decrease in the thickness of the bone trabeculae which, however, are normally calcified. Several investigators have attempted to analyze the mechanism which leads to these anatomic changes by measuring metabolic balances (1, 2). Indeed, great strides have been made, since such studies have shown that the skeleton undergoes constant changes of demineralization and new bone formation. It was realized (3, 4) that the building blocks of bone, such as protein and minerals, have to be provided in adequate amounts; that the absorption and utilization of these food substances have to take place in a suitable environment with the aid of enzymes and vitamins, mainly vitamin D. It was found that the hormones of the parathyroid gland, of the adrenal cortex, of the gonads and of other glands exert a controlling influence upon the maintenance of the normal bone structure. Also, it was recognized that muscular activity is a strong stimulus for bone formation.

When, under the influence of any of these factors, the process of demineralization or of bone apposition is accelerated for a sufficient period of time, changes in the density of bone will become apparent roentgenographically. It is known that the skeleton must lose or gain about 30 per cent of its mineral content before significant changes in the density become apparent upon x-ray examination (5); therefore, it may take years until appreciable roentgenographic abnormalities can be noted.

The serum levels of calcium, phosphorus and alkaline phosphatase, and the Sulkowitch test for urinary calcium provide helpful, although only limited, information regarding the patho-physiology of bone. For the characterization of metabolic bone disease one would like to be able to determine the skeletal mass, the turnover rate of minerals and proteins, the size of their metabolic pool, the extent of demineralization and the extent of bone apposition. One can measure the mineral and nitrogen balances, but such a study requires special facilities which are not readily available.

A calcium tolerance test, a simple tool to study calcium balance, has been recently described; it appears to furnish information regarding the magnitude of demineralization and of mineral deposition separately (6, 7). A low calcium

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TABLE 1. *Calcium Tolerance Test*

*Average Urinary Calcium Excretion on the Day Prior to, and on the Day of Test*

| Group | Urinary calcium excretion mg./24 hrs. | |
|---|---|---|
| | Spontaneous* | Induced** |
| A | 27 | 58 |
| B | 71 | 200 |
| C | 202 | 423 |

* Urinary calcium excretion on the day prior to the test.

** Urinary calcium excretion on the day of the test (infusion of 446 mg. of calcium).

TABLE 2. *Schematic Presentation of Factors Influencing Spontaneous and Induced Calcinuria*

| Calcium balance | | Calcinuria mg./24 hrs. | | | Retention of infused calcium (446 mg.) | |
|---|---|---|---|---|---|---|
| | | Spontaneous | Induced* | Excess | mg. | Utilization % |
| Normal | | 70 (−170 + 100)** | 200 | 130 | 316 | 71 |
| Demineralization | A | 170 (*−270* + 100) | *300* | 130 | 316 | 71 |
| | B | 170 (−170 + **0**) | *400* | 230 | 216 | *49* |

* Calcinuria on the day of the test.

** Figures in parentheses represent the amount of calcium assumed to be released by osteoclastic activity (negative values) and re-utilized for bone formation (positive values). The difference between the two is assumed to represent spontaneous calcinuria.

diet containing approximately 150 mg. of calcium and 600 mg. of phosphorus is given for three days preceding the test and for three days of the test. An infusion of 50 cc. of 10 per cent calcium gluconate (containing 446 mg. of calcium) in 500 cc. of 5 per cent glucose in water is given in the fasting state over exactly four hours. The 24-hour urinary calcium[1] is determined on the day prior to, on the day of, and on the day after the test. The intravenous route eliminates differences due to the variability of intestinal absorption. Since the intravenously administered calcium is mainly excreted in the urine (8, 9), the difference between the intake (the infused dose) and the output (the excess urinary calcium excretion) is the balance. This test has been performed in approximately 100 patients and three distinct patterns of urinary calcium excretion have been noted on the day of the test: 1) normal, Group B, 2) indicative of mineral retention, Group A, and 3) indicative of increased demineralization, Group C (Table 1).

The information which this test can furnish is illustrated schematically in Table 2. The figures listed under "normal" are those of a subject whose calcium balance

[1] The urinary calcium was determined according to the method of Shohl and Pedley, *J. Biol. Chem.* **50:** 537, 1922.

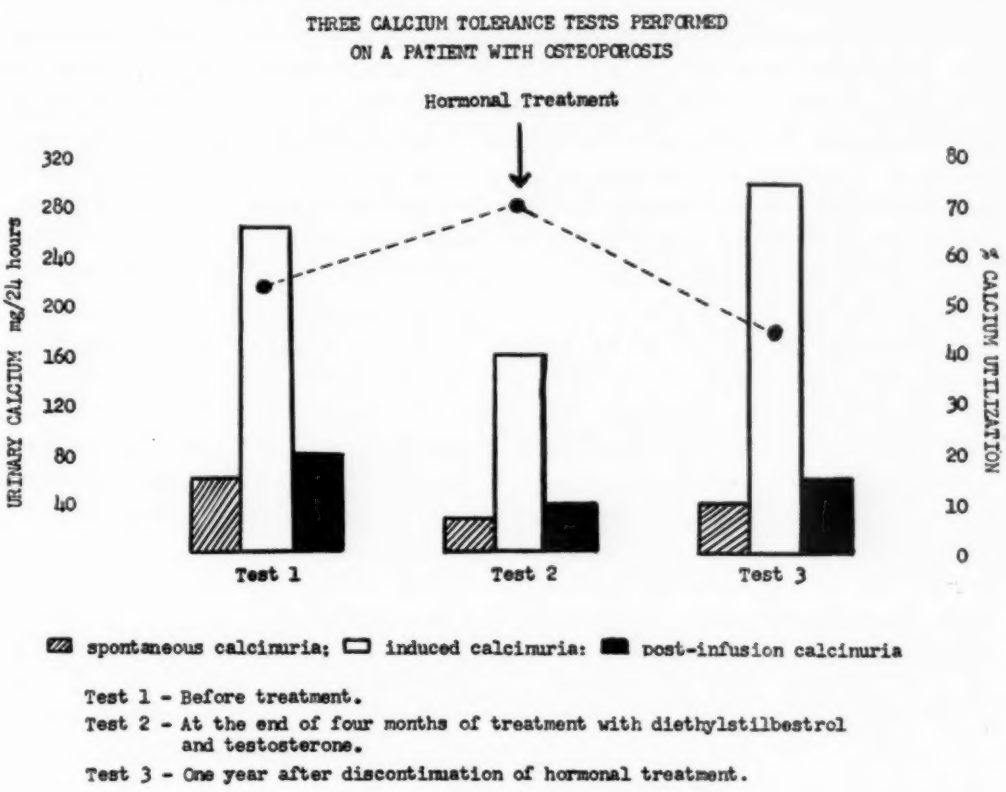



FIGURE 1

was in near-equilibrium on a low calcium intake. Patient A and Patient B were in negative calcium balance, as indicated by the increased spontaneous calciuria, which was equally high in both patients. However, the mechanism responsible for this mineral loss may have been different, namely, increased osteoclastic activity in Patient A, and decreased osteoblastic activity with an unchanged rate of demineralization in Patient B. This becomes apparent upon noting the difference between the utilization rates of the infused calcium. The utilization was 71 per cent in the normal subject and in Patient A, whereas it was decreased to 49 per cent in Patient B. The disturbance of mineral metabolism in senile osteoporosis is assumed to be similar to that of Patient B, whereas the pattern seen in hyperparathyroidism is similar to that of Patient A.

Ten patients with senile osteoporosis were studied with the aid of this test. Figure 1 shows the results of three tests which were performed on one of these patients before treatment, at the end of four months of hormonal treatment, and one year after its discontinuation. The result of the second test was distinctly different from that of the first and third tests. The utilization rate of the infused calcium was lower than normal (54 per cent and 45 per cent, respectively) in tests 1 and 3, and became normal (70 per cent) after hormonal therapy. The low rate of utilization prior to treatment points to a deficiency of osteoblastic activity, as illustrated by Patient B in Table 2. In spite of extensive roentgenographic changes in the skeleton, there was no detectable abnormality in the serum levels

of calcium, phosphorus and alkaline phosphatase and of the calcium balance of this patient. Normal mineral and protein balances have been repeatedly observed in patients with senile osteoporosis. This may be due to the fact that the abnormal process of demineralization secondary to decreased osteoblastic activity proceeds so slowly over a prolonged period of time, possibly over many years, as to remain undetected. By loading the system with excess calcium, as in this test, aberrations of calcium metabolism may become apparent.

In other instances of osteoporosis the mineral balances are negative, as in Patient B (Table 2). Due to the lack of new bone formation, the mineral losses must finally lead to exhaustion of the mineral depots, so that the x-ray shadows of bones resemble those of soft tissue. At this stage, the skeleton may have become so demineralized that only minimal amounts are available for further loss and the mineral balances may again become "normal." Only when techniques become available which will determine the rate of demineralization and the skeletal mass, will it be possible to differentiate cases of rapid mineral loss reaching the final stage from those of slow, prolonged demineralization.

The improvement in the utilization of calcium with hormonal treatment indicates hormonal stimulation of osteoblastic activity (10, 11). Moreover, metabolic balances performed on this patient at the end of hormonal treatment showed the marked anabolic effect of stilbestrol and testosterone on protein metabolism (Table 3). The balances of nitrogen, phosphorus and potassium became markedly positive. The calcium balance was slightly negative, as is also found in normal subjects, on a low calcium intake.

The metabolic balances and the results of the calcium tolerance test performed in the other 9 patients with senile osteoporosis agreed in some cases with the schematic outline of the pattern of Patient B (Table 2), but others were in line with the pattern of the stage of exhaustion.

Once severe demineralization has occurred, regardless of the time-span required for its development, clinical symptoms of osteoporosis may appear. These may be nonspecific, such as general debility, or they may be related to the skele-

TABLE 3. *Metabolic Balance Study of a 60-Year-Old Female Patient with Osteoporosis*

(Observation for eighteen days at the completion of four months' treatment with diethylstilbestrol, 1 mg. per day, and testosterone propionate, 12.5 mg. three times per week)

| | Intake (mg. or mEq.) | Output | | Balance (mg. or mEq.) | Serum levels* (mg./100 ml. or mEq./L) |
|---|---|---|---|---|---|
| | | Urine (mg. or mEq.) | Stool (mg. or mEq.) | | |
| Nitrogen | 9312 | 5827 | 1024 | +2461 | – |
| Phosphorus | 610 | 244 | 213 | +153 | 2.7 |
| Potassium** | 52 | 28 | 8 | +16 | 4.5 |
| Calcium | 149 | 38 | 170 | −59 | 9.4 |

* Alkaline phosphatase, 3.2 B.U.

** K in mEq.

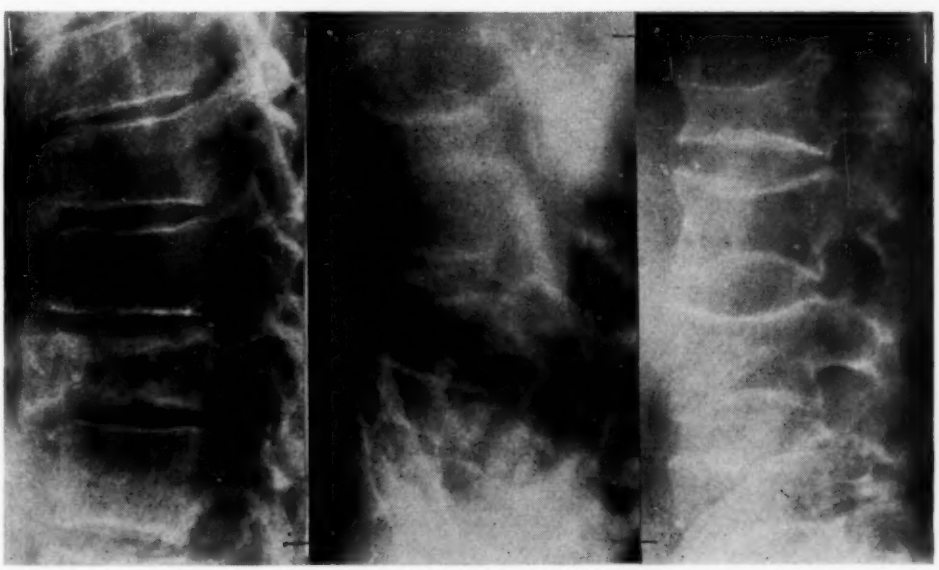
tal system, such as bone pain and fractures. Since senile osteoporosis occurs in the age-group with the highest incidence of malignancy, the differential diagnosis of malignancy affecting the skeleton, and osteoporosis, may at times be difficult. The x-ray appearance may be similar or even indistinguishable. Errors in diagnosis have been reported (12).

Two brief case histories illustrate such errors. Both patients were admitted with the diagnosis of terminal metastatic malignancy. No malignancy was found and the changes in the bone were revealed to be due to senile osteoporosis.

*Case 1:* An 82-year-old female (M.H. 54833) had noted painless swelling of the abdomen for six months. A large firm abdominal mass, ascites and a left pleural effusion were noted. X-ray examination of the osseous structures showed partial collapse of D-11 and several poorly defined areas of decreased density of the skull, suggestive of bone metastases (Fig. 2-A). On exploration, a large benign fibroma of the ovary was found. There was no evidence of malignancy anywhere.

*Case 2:* A 64-year-old male (M.H. 42835) was admitted for terminal care, with a diagnosis of generalized carcinomatosis secondary to a neoplasm of the lung. The patient had shortness of breath and pain in the lower back and hip. X-ray examination of the chest showed an area of infiltration in the lower right lung field. Compression of the 4th lumbar vertebra and areas of decreased density of the skull were thought to be due to metastases to bone. However, this patient had no tumor, but had advanced generalized osteoporosis with codfish vertebrae of the lumbar spine (Fig. 2-B). On bronchoscopy, a redundant flap of mucosa was found which partially occluded the right main bronchus, causing recurrent attacks of pneumonitis.

Conversely, the error can be made of diagnosing senile osteoporosis when, in fact, the disease of the bone is due to malignancy. Well known is the difficulty in differentiating multiple myeloma (Fig. 2-C) from generalized osteoporosis (13).



A B C

FIG. 2. A = Case 1; B = Case 2; C = Multiple myeloma

Even more serious is the error which can be made when tumor and osteoporosis coexist, so that a primary operable malignant tumor may be considered inoperable on the basis of skeletal changes. Older patients with operable malignant tumors and osteoporosis may be denied surgery because of the assumption of metastatic malignancy to bone.

## SUMMARY AND CONCLUSIONS

With the extension of the average life span, chronic diseases and diseases occurring in the aged become increasingly important medical problems. A great deal of attention is being paid by clinicians and investigators to the changes which occur in senescence. Whether such changes represent disease states, or are the inevitable sequelae of "wear and tear" is at present impossible to decide. This also applies to senile osteoporosis. Attempts to prevent osteoporosis by hormonal supplementation have to be given serious consideration, keeping in mind the possible side effects of such prolonged treatment on tissues other than the skeleton.

The mechanism leading to senile osteoporosis has been studied (1, 14, 15). It is assumed that gonadal factors and skeletal inactivity play an important role in its development. However, a decline in blood supply due to degenerative vascular changes, impairment of capillary distribution and altered permeability of the capillary wall affecting the exchange of nutrients and waste products, may also be contributing factors. No systematic investigations seem to have been performed regarding the possible role of impaired vascularization, although avascularity has been noted in bone specimens of the aged (16, 17).

With the availability of a relatively simple method to test certain aspects of calcium metabolism in man, it may be hoped that "asymptomatic" early cases of osteoporosis will be recognized before disease states develop. The evaluation of prophylactic or therapeutic measures may also be promoted with the aid of this test.

*Acknowledgment*

We wish to express our appreciation for the assistance given by Mrs. Vernice Vankinscott, R.N. and Miss Estelle D. Gottesman, research dietitian.

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# STEROID STUDIES. I. METABOLIC EFFECTS OF ANDROSTANOLONE IN AGED PEOPLE

SIDNEY PEARSON, PH.D., JONAS WEISSBERG, M.D. AND THOMAS H. McGAVACK, M.D.

*The New York Medical College, Metropolitan Hospital, Research Unit, Welfare Island, New York 17, N. Y.*

## INTRODUCTION

It has been reported that androstanolone, *i.e.*, androstan-17($\beta$)-ol-3-one, has renotropic (1, 2) antifibromatogenic (3, 4) and luteoid (5) activity. As an androgen, Kochakian (1) found androstanolone to be equal to testosterone and testosterone propionate in castrated mice. However, Escher and his associates (6), who found androstanolone useful for the treatment of human mammary cancer, stated that the androgenic effect of androstanolone in the human being was minimal as compared with that of the testosterones.

Metabolically, androstanolone has produced an increase in kidney arginase (7) and has caused nitrogen retention (8, 9) in castrated mice.

This report describes some metabolic effects following administration of androstanolone[1] to aged people.

## PROCEDURE

The patients selected for this study were:

A. A 59-year-old male with a history of occasional epileptic spells.
B. A 65-year-old male with hypertension.
C. A 55-year-old female with Parkinsonism.
D. A 62-year-old female with advanced arteriosclerosis, particularly of both feet.
E. A 58-year-old male with generalized arteriosclerosis and transient hemiparesis (three months previously).
F. A 75-year-old male with relatively inactive osteoarthritis.

For twenty days, the patients received a constant daily diet which contained an average of 83 Gm. of protein, 71 Gm. of fat and 322 Gm. of carbohydrate; the caloric content averaged 2,262 calories.

Patients who had been in the hospital and on the ward diet for several months or more were chosen for the study. The exception to this, was Patient E, who was a "last minute" replacement for the original fifth subject. Patient E had received the ward diet for about three days before the beginning of the study. The food given to the patients closely approximated the ward diet, so that any effects due to adjustment to diet might be minimized.

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[1] We wish to thank Dr. A. White of Chemical Specialties Co., Inc., New York, who supplied the androstanolone used in this work. This compound has been referred to in the literature as -17($\alpha$)-ol instead of -17($\beta$)-ol.

After a four-day control period during which no drug was given, the subjects received intramuscular injections of 0, 25, 50 or 100 mg. of androstanolone daily for twelve days. During the final four days of study, the recovery period, no drug was given to any subject. Patients A and E received androstanolone for thirteen instead of twelve days, and were allowed a three-day recovery period.

Every two days, two-day aliquots of food were analyzed for sodium, potassium, chloride and nitrogen. The average daily intakes were:

| | |
|---|---|
| Sodium | 101 ± 10.6 mEq. |
| Potassium | 89 ± 5.1 mEq. |
| Chloride | 111 ± 8.9 mEq. |
| Nitrogen | 12.5 ± 0.6 mEq. |

Forty-eight-hour urinary specimens were analyzed for sodium, potassium, chloride, nitrogen, 17-ketosteroids and creatinine; determinations were made on blood for concentration of sodium, potassium, chloride, total cholesterol, total serum protein, albumin, and globulin at the end of the control period, at the middle and again at the end of the period of steroid administration, and finally at the end of the period of recovery. The procedure of Drekter and his associates was used for the determination of 17-ketosteroids (10).

The subjects were weighed daily at 7 A.M.

FIG. 1 EFFECT OF ANDROSTANOLONE ON NITROGEN BALANCE

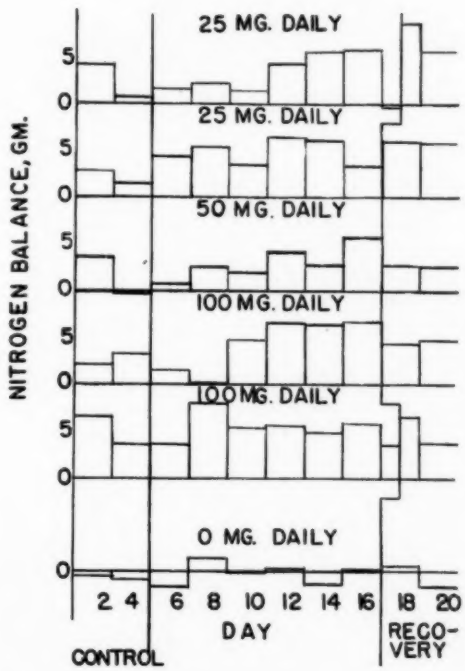


FIGURE 1

TABLE 1. *Electrolyte Balances (Food Intake Minus Urinary Excretion) for 2-day Periods, in Subjects Receiving Varying Doses of Androstanolone*

| | Patient & dose of androstanolone | Day of study | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Control | | Androstanolone | | | | | | | Recovery period | | |
| | | 1, 2 | 3, 4 | 5, 6 | 7, 8 | 9, 10 | 11, 12 | 13, 14 | 15, 16 | 17* | 17, 18 | 18 | 19, 20 |
| Sodium, mEq. | $A_{25}$** | −38 | +24 | +45 | — | −27 | +108 | +96 | +36 | −79 | — | +98 | +89 |
| | $B_{25}$ | +106 | +64 | +61 | — | +93 | +81 | +66 | +89 | — | +76 | | +89 |
| | $C_{50}$ | +63 | +46 | +48 | — | +35 | +41 | +81 | +81 | — | +21 | — | +36 |
| | $D_{100}$ | +55 | +54 | −2 | — | +81 | +67 | +122 | +71 | — | +11 | — | −48 |
| | $E_{100}$ | +41 | +64 | +93 | — | +78 | +53 | +26 | +28 | +14 | — | +36 | +29 |
| | $F_0$ | −152 | −38 | +64 | — | −59 | +21 | −13 | −19 | — | −7 | — | +39 |
| Potassium, mEq. | $A_{25}$ | +62 | +80 | +76 | — | +65 | +79 | +89 | +78 | +29 | — | +60 | +90 |
| | $B_{25}$ | +5 | +85 | +87 | — | +106 | +98 | +106 | +71 | — | — | +97 | +88 |
| | $C_{50}$ | +93 | +78 | +80 | — | +80 | +94 | +68 | +78 | — | +38 | — | +78 |
| | $D_{100}$ | +90 | +73 | +80 | — | +82 | +72 | +96 | +92 | — | +43 | — | +150 |
| | $E_{100}$ | +90 | +89 | +97 | — | +63 | +76 | +63 | +72 | +19 | — | +17 | +73 |
| | $F_0$ | +54 | +61 | +85 | — | +44 | +67 | +26 | +51 | — | +9 | — | +45 |
| Chloride, mEq. | $A_{25}$ | −11 | +21 | +6 | — | −32 | +94 | +123 | +71 | −86 | — | +125 | +185 |
| | $B_{25}$ | +148 | +75 | +83 | — | +125 | +109 | +88 | +91 | — | — | +118 | +94 |
| | $C_{50}$ | +71 | +1 | +39 | — | +40 | +66 | +76 | +92 | — | — | +11 | +74 |
| | $D_{100}$ | +66 | +5 | −8 | — | +59 | +66 | +109 | +83 | — | — | +22 | +55 |
| | $E_{100}$ | +46 | +26 | +71 | — | +72 | +43 | +36 | +29 | +15 | — | +26 | +53 |
| | $F_0$ | — | −6 | +6 | — | −67 | +44 | +23 | −13 | — | — | −12 | +37 |

* Patients A and E received androstanolone for 13 days instead of 12 days. In these cases values for the 17th and 18th days are daily, not 2-day values.

** Daily dose (mg.) of androstanolone.

TABLE 2. *Total 2-Day Urinary Excretions in Subjects Receiving Androstanolone*

| Patient & dose of androstanolone | Total 17-ketosteroids (mg.-equivalents)† | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Day of study | | | | | | | | | | | |
| | Control | | Androstanolone | | | | | | | Recovery period | | |
| | 1, 2 | 3, 4 | 5, 6 | 7, 8 | 9, 10 | 11, 12 | 13, 14 | 15, 16 | 17* | 17, 18 | 18 | 19, 20 |
| $A_{25}$** | 18.4 | 15.6 | 28.4 | 17.1 | 27.4 | 19.5 | 19.6 | 19.5 | 23.1 | | 4.1 | 16.5 |
| $B_{25}$ | 14.5 | 15.7 | 20.2 | 13.4 | 14.4 | 15.6 | 16.2 | 20.4 | | 14.5 | | 13.4 |
| $C_{50}$ | 20.3 | 13.9 | 27.1 | 30.5 | 41.8 | 42.6 | 49.5 | 56.5 | | 36.5 | | 61.5 |
| $D_{100}$ | 10.2 | 9.4 | 19.9 | 20.9 | 28.1 | 32.0 | 38.0 | 44.7 | | 111 | | 39.2 |
| $E_{100}$ | 16.4 | 17.2 | 30.9 | 43.1 | 53.3 | 86.0 | 74.7 | 62.4 | 38.6 | | 32.9 | 53.2 |
| $F_0$ | 30.9 | 23.8 | 31.4 | 23.6 | 29.6 | 30.7 | 36.7 | 32.4 | | 31.0 | | 28.3 |
| | Creatinine (mg.) | | | | | | | | | | | |
| $A_{25}$ | 1.9 | 2.3 | 2.7 | 2.2 | 2.6 | 2.1 | 1.4 | 1.6 | 1.6 | | 0.43 | 1.5 |
| $B_{25}$ | — | — | — | — | — | — | — | — | — | — | — | — |
| $C_{50}$ | 1.5 | 1.9 | 1.9 | 2.1 | 2.0 | 1.8 | 2.0 | 1.9 | — | 2.1 | — | 2.0 |
| $D_{100}$ | 1.5 | 1.5 | 1.5 | 2.2 | 1.4 | 1.2 | 1.5 | 1.5 | — | 1.8 | — | 1.8 |
| $E_{100}$ | 1.4 | 2.0 | 2.0 | 1.0 | 2.1 | 1.9 | 2.1 | 1.7 | 0.71 | — | 0.92 | 2.0 |
| $F_0$ | 2.9 | 2.5 | 2.9 | 3.1 | 2.5 | 2.2 | 2.5 | 2.4 | — | 2.5 | — | 2.4 |

† One mg.-equivalent is that amount of steroid which is equal to 1 mg. of dehydroisoandrosterone when assayed by the modified Zimmermann reaction (10).

* See footnote to Table 1.

** Daily dose (mg.) of androstanolone.

## RESULTS

Androstanolone produced nitrogen retention in Subjects A, B, C and D, who received 25, 50 or 100 mg. daily, respectively (Fig. 1). There was an interval of about four to six days between the initial injection and the appearance of an increase in the retention of nitrogen. The increased nitrogen balance was accompanied by an increase in weight of from 3 to 5 pounds in each subject, except in Patient A who showed no concomitant change in weight. However, on the seventeenth day, Patient A had a temperature of 101° F. and his previously positive nitrogen balance became slightly negative. Subject E was already retaining large amounts of nitrogen when the administration of androstanolone was begun; doses of 100 mg. daily did not further increase his retention (Fig. 1).

TABLE 3. *Effect of Androstanolone on Blood Constituents*

| Patient & dose of androstanolone | Day of study* | Na (mEq./L) | K (mEq./L) | Cl (mEq./L) | Cholesterol (mg./100 ml.) | Protein, (Gm./100 ml.) | Alb. (Gm./100 ml.) | Glob. (Gm./100 ml.) | A/G |
|---|---|---|---|---|---|---|---|---|---|
| $A_{25}$** | 4 | 134 | 4.0 | 103 | 242 | 6.5 | 4.5 | 2.0 | 2.2 |
| | 9 | 136 | 4.3 | 107 | 255 | 6.5 | 4.4 | 2.1 | 2.1 |
| | 16 | 134 | 4.5 | 103 | 269 | 6.7 | 4.4 | 2.3 | 1.9 |
| | 20 | 136 | 3.8 | 112 | 237 | 7.0 | 5.3 | 1.7 | 3.1 |
| $B_{25}$ | 4 | 144 | 5.2 | 113 | 260 | 6.9 | 4.1 | 2.8 | 1.5 |
| | 9 | 132 | 4.6 | 104 | 235 | 7.5 | 5.4 | 2.1 | 2.6 |
| | 16 | 142 | 4.8 | 110 | 237 | 6.8 | 4.8 | 2.0 | 2.4 |
| | 20 | — | — | — | — | — | — | — | — |
| $C_{50}$ | 4 | 130 | 4.3 | 102 | 312 | 7.5 | 5.0 | 2.5 | 2.0 |
| | 9 | 132 | 4.7 | 103 | 258 | 6.7 | 4.4 | 2.3 | 1.9 |
| | 16 | 134 | 4.2 | 102 | 248 | 6.7 | 4.8 | 1.9 | 2.5 |
| | 20 | 134 | 4.3 | 112 | 260 | 6.9 | 5.0 | 1.9 | 2.6 |
| $D_{100}$ | 4 | 130 | 4.8 | 103 | 242 | 7.0 | 3.8 | 3.2 | 1.2 |
| | 9 | 128 | 4.9 | 104 | 228 | 6.6 | 3.8 | 2.8 | 1.4 |
| | 16 | 138 | 4.7 | 104 | 246 | 6.8 | 4.1 | 2.7 | 1.5 |
| | 20 | 136 | 4.5 | 108 | 271 | 7.4 | 4.7 | 2.7 | 1.7 |
| $E_{100}$ | 4 | 132 | 4.7 | 103 | 139 | 7.2 | 4.5 | 2.7 | 1.7 |
| | 9 | 130 | 4.4 | 98 | 131 | 7.5 | 4.5 | 3.0 | 1.5 |
| | 16 | 138 | 5.0 | 103 | 130 | 7.6 | 4.2 | 3.4 | 1.2 |
| | 20 | 132 | 4.3 | 107 | 134 | 7.9 | 5.0 | 2.9 | 1.7 |
| $F_0$ | 4 | 126 | 4.6 | 101 | 160 | 8.0 | 4.4 | 3.6 | 1.2 |
| | 9 | 126 | 4.8 | 108 | 225 | 6.7 | 4.3 | 2.4 | 1.8 |
| | 16 | 139 | 4.7 | — | 226 | 6.8 | 4.2 | 2.6 | 1.6 |
| | 20 | 132 | 4.2 | 111 | 227 | 7.1 | 5.1 | 2.0 | 2.6 |

* 4th day = last day of control.
9th day = 5th day of androstanolone.
16th day = 12th and last day of androstanolone.
20th day = last day of recovery period.
** Daily dose (mg.) of androstanolone.

Androstanolone had no significant effect on the excretion in the urine of sodium, potassium, chloride and creatinine (Tables 1 and 2), or on the constituents of the serum which were measured (Table 3).

There was an increase in the urinary 17-ketosteroid excretion of patients who received 50 mg. or 100 mg. of androstanolone daily, but none in those subjects who were given 25 mg. daily (Table 2).

In all cases, androstanolone produced a marked feeling of well being.

## DISCUSSION

A varied response to androstanolone was observed. This steroid increased nitrogen retention at three dosage levels, 25 mg., 50 mg., and 100 mg. However, in one instance, Patient E, 100 mg. showed no such activity (Fig. 1). Patient E had been on the ward for only three days before the study was begun. During the control period, there was a highly positive nitrogen balance. This initially high nitrogen balance was probably in the nature of a maximal response to adequate food following his previously poor nutritional habits, and may account for the apparent failure of androstanolone to alter his nitrogen balance further.

Based on our experience, the steroids testosterone propionate, androstanolone and $\Delta^4$-androstenedione-3,17 show a decreasing ability, in the order listed, to produce nitrogen retention when given to aged people. This is the same relative order of activity reported by Kochakian (9), who studied the effect of these steroids on the nitrogen balances of castrated rats.

An increase in the urinary excretion of 17-ketosteroids was observed in all patients who received 50 or 100 mg. of androstanolone daily, but not in those receiving 25 mg. daily. There is good evidence (11) to suggest that the administration of androstanolone disturbs the pattern of 17-ketosteroid excretion. From this evidence it appears that one or both of two things may occur: 1) androstanolone is changed to some other metabolite of the "17-ketosteroid group," in whole or in part, before it is excreted, or 2) androstanolone is capable of suppressing in whole or in part, in proper dosage, the formation of 17-ketosteroids by the body. Both of these mechanisms are probably at work. Simultaneously, we realize that still other factors may be concerned and that dosage itself may prove to be important.

## SUMMARY

1. In 4 of 5 subjects varying in age from 55 to 65 years, androstanolone was shown to cause nitrogen retention in doses as low as 25 mg. daily.

2. Androstanolone had no effect on urinary sodium, chloride, potassium and creatinine excretion, or on any of a number of constituents of the blood which were studied.

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# PRINCIPLES IN THE MANAGEMENT OF THE AGED SURGICAL PATIENT

SIDNEY E. ZIFFREN, M.D. AND STUART C. CULLEN, M.D.

*The Department of Surgery, the State University of Iowa College of Medicine, Iowa City, Iowa*

We have previously described in detail the preparation of the aged patient for emergency surgery (1). The present paper deals exclusively with the management of the non-emergency elderly patient.

## THE PREOPERATIVE PERIOD

If the aged patient has a normal blood count, appears hydrated, and needs surgery of a non-exhausting character such as an inguinal hernioplasty, no extensive preparation is needed. However, if the patient has a disease process requiring extensive surgery such as a bowel resection, gastric resection, or pulmonary resection, he will usually need preoperative preparation.

As has been pointed out before (2, 3), a deficient blood volume is a constant hazard which must be recognized and treated in the aged patient. If the patient has a normal blood count or blood plasma protein level, the clinician too often assumes the blood volume is satisfactory. Blood volume studies are not established as a routine, and their accuracy is often open to question. Nevertheless, the patient who has a serious surgical disease, such as malignancy of the bowel, will very frequently have a reduced blood volume. To operate upon him under such circumstances is to deal recklessly with his life. A small blood loss on the operating table may precipitate shock in such a patient. Sometimes this is rectifiable, but too often the diminished physiologic reserve of the patient cannot withstand the anoxic state and an irreversible situation develops.

What is often surprising in many of these elderly, ill patients is to find, for example, a hemoglobin level of 12 to 13 Gm. per 100 ml. and a red blood cell count of over 4 million per cu. mm.; following the administration of 1,000 ml. of blood, the new hemoglobin level is only 10 Gm. per 100 ml. and the red blood cell count is below 4 million per cu. mm. Such an initial blood count is not an error, but only a manifestation of reduced volume with hemoconcentration. After the first transfusion of 500 ml. of blood the patient improves. He begins to drink and to eat and overcomes his dehydration; with a second blood transfusion he improves still more. The consequent lowered blood count is then evident. The last count is closer to the truth.

One may well ask, how much blood is necessary? No definite rule can be given. The general appearance of the patient, the color and turgor of his skin, and his well being must be taken into consideration. It is surprising how soon the clinician who pays close attention to this problem in the elderly patient can tell when he has in large measure overcome the blood volume deficit.

Fluid replacement is no problem in the patient who drinks freely and who displays none of the signs of dehydration. However, the patient who, for example,

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has pyloric obstruction or refuses to eat or drink must be adequately hydrated. In this connection it is well to remember that one of the causes of low blood volume is dehydration. The great difficulty in the management of dehydration is the commonly accepted view that the aged patient requires as much fluid as does a younger person for the ordinary demands of insensible fluid loss and urinary output. An interesting clinical fact is that, if an elderly person is watched from day to day, it will be noted that the amount of fluid which is consumed is surprisingly low. The insensible daily loss is probably smaller than the commonly accepted 1,000 ml.; a more accurate figure is probably 500 ml. The minimal amount of fluid needed for a kidney which is operating at a good capacity is about 600 ml. per day. Assuming that its function is somewhat impaired, we may postulate a figure of 1,000 ml. per day. The aged patient then probably requires about 1,500 ml. of fluid daily. If he is dehydrated, naturally a larger quantity is needed. One index is the kidney output. It is probable that most of the fluid requirement of the cells is met before the kidneys receive fluid for excretory purposes. If the daily urinary output is 1,000 ml., it can be reasonably assumed that dehydration has been relieved. This does not necessarily mean that an aged patient needs enough fluid to put out 1,000 ml. of urine each day.

For specific rehydration purposes, when the patient cannot take fluids by mouth, there is no better fluid than 5 per cent dextrose in distilled water. The surgeon must not permit himself to be confused by the patient who has edema, yet may be dehydrated. Ordinarily this condition is due to heart failure, and correction of the cardiac insufficiency will relieve the edema. The excess salt which is holding the water in the extracellular space will be gradually eliminated as the cardiac status improves.

There is a considerable body of evidence opposing the use of hypodermoclysis for parenteral fluid administration (4). Unless the fluid given by the subcutaneous route contains an electrolyte and is isotonic with the blood, it must cause the withdrawal of fluid from the other body stores, including the blood, in order that it may be brought into balance with the plasma before it can be absorbed. Disastrous results may be expected in some aged, dehydrated patients who are administered a non-electrolyte solution by hypodermoclysis. The intravenous route is preferable.

Before surgery, electrolytes are needed only if the patient has been vomiting, has had diarrhea or a fistula, or is undergoing constant aspiration from the gastrointestinal tract. The body tends to conserve electrolytes in the patient with a properly functioning kidney. However, if one of the foregoing complications has existed over several days, replacement will be necessary. Three items will be needed—sodium, potassium and chloride. Physiologic salt solution is 0.9 per cent; thus 1,000 ml. contains 9 grams of salt or 154 milliequivalents each of sodium and chloride. It is a safe rule in treating the geriatric patient to assume that fluid from gastrointestinal aspiration contains approximately 6 grams of sodium chloride per liter. The amount of such aspirate or vomitus can be replaced by using a proportion of $\frac{2}{3}$ saline to $\frac{1}{3}$ dextrose in water. In addition, it may be necessary to replace potassium. In the gastric juice its concentration approximates 9 milliequivalents per liter. If potassium is administered in the amount of 2 or 3 grams

(30–40 mEq.) for each 1,500 ml. of aspirate, this should more than compensate for the current potassium loss. With diarrhea, the loss may be greater and replacement necessarily cannot be as quantitative or as accurate. The use of physiologic sodium chloride along with potassium is necessary under these circumstances for restoration.

The replacement of electrolytes requires certain precautions. No attempt should be made to introduce large quantities of saline solution without first replenishing the blood volume. Blood contains not only red blood cells but protein and electrolyte as well. It also helps the patient with a low protein level to overcome the tendency to retain salt, thus avoiding water retention and edema. Above all, overestimation of the loss must be avoided; otherwise, the risk of overloading the patient with salt, with consequent edema (especially pulmonary) is a hazard constantly facing the patient. Potassium should be administered slowly. Before it is used one must ascertain if the patient has an adequate urinary output. Furthermore, the patient who has a heart block must not be subjected to the too-rapid administration of potassium. If the patient can take fluids by mouth the risks of electrolyte administration are minimized, as the oral route for ingestion of fluids is far superior to parenteral injection; oral ingestion will rapidly and more adequately correct the body deficiency.

Of all the phases of preoperative management, nutrition is probably the most neglected and the least understood. There is a popular conception that administration of a few bottles of protein hydrolysate with glucose can correct malnutrition. A few essential facts will refute this concept. It is very difficult, by conventional methods, to restore the protein and glycogen stores of the body by means of parenteral fluids. It is most important first to restore blood volume by means of blood transfusions before the benefits of intensive nutritional therapy can be attained (5). When intensive therapy is started, vitamins must be administered in large quantities. Vitamins participate in the metabolism of food and during starvation the body need for vitamins is reduced. When calories are supplied, however, the depleted stores are rapidly utilized and acute signs of deficiency appear.

By far the most suitable and effective means of supplying material needed for restoring the nutritional status is by the oral route. Restoration may thus be accomplished by increasing the amount of food eaten, by giving whiskey before meals as a stimulus, by supplemental feedings, by formula feedings, or by injection of a rich formula through an indwelling polyethylene tube in the stomach. An index to improved nutrition is the muscular power of the individual and his general weight gain and appearance.

In order to improve nutritional status by parenteral methods, vigorous measures are necessary. Normally, the resting individual requires about 1,500 calories per twenty-four hours to maintain his weight. A still greater caloric intake is required, in order to increase the body stores. The usual 5 per cent protein hydrolysate in 5 per cent dextrose theoretically should contain 50 Gm. of protein in 1,000 ml. The manufacturer, however, only claims 38 Gm. of protein equivalent and states that 1,000 ml. supplies 355 calories. If the solution, in addition, con-

tains 5 per cent alcohol, it supplies approximately 710 calories per liter. If the simple protein hydrolysate in dextrose is used it will require about 4 liters a day to supply the ordinary daily caloric requirement, without any opportunity for increasing body stores. If the solution containing alcohol is used, it must be administered very slowly; it means long periods of immobilization, to which the elderly patient soon objects. It has been the experience of most individuals that in order to introduce by the parenteral route large quantities of protein and carbohydrate for the purpose of increasing the body stores, a 24-hour continuous drip must be used. The conventional method of administration through a regular intravenous needle is unsatisfactory. A small polyethylene tube threaded into the basilic vein can be used satisfactorily for several days (6). With this method, solutions of even greater caloric value can be administered. For instance, to the alcohol-hydrolysate-dextrose mixture, 50 ml. of 50 per cent dextrose may be added, so that each 1,050 ml. will contain approximately 900 calories. In a patient with a benign obstructive lesion of the pylorus, a preliminary jejunostomy allows formula feedings, and nourishment supplied in this way is even more effective than that given by the parenteral route. There is no doubt that, as yet, we have no simple means of parenteral alimentation that can substitute for the introduction and assimilation of food through the gastrointestinal tract.

## ANESTHESIA

Anesthesia for the aged patient is a special problem, only because these patients do not have the respiratory and circulatory reserve possessed by most of the younger patients. The ability of the aged patient to compensate for depression of respiration and circulation is appreciably diminished. As a result, it is the responsibility of the anesthetist to avoid any more depression than just the amount required for the particular procedure, and to be in a position at all times to reverse the depressed state which he induces in the patient.

The choice of anesthetic agent and technic in the elderly patient is made by using the same factors that are utilized in the selection of anesthetic agents for any patient. These factors include the requirements of the surgical procedure, the physical state of the patient, and his comfort. It is especially important in the elderly, however, to select the anesthetic on an individual basis. There is no well controlled evidence to indicate that spinal analgesia, infiltration or regional analgesia, or any of the particular inhalation or intravenous agents are "ideal" agents or technics for the older person. Any of the drugs and methods employed in anesthesia may be employed in the aged, provided they are applied with special reference to the requirements of surgery, the physical state, and the comfort of the particular patient in which they are used.

For example, there is no well controlled evidence which indicates that, in the elderly patient, local anesthesia is the best choice for hernioplasty, that spinal analgesia is the best choice for amputations, or that nitrous oxide anesthesia, with or without adjunctive drugs such as pentothal, is the best choice for celiotomy. There is no justification for employing a specific drug or method in all aged persons, simply because they are old; there are many other factors influencing

the choice of anesthetic. For example, in one elderly patient requiring herniorrhaphy, infiltration or regional analgesia may be better because the patient is cooperative, he is thin, and the hernia is easily reduced. In another patient spinal analgesia may be better because he is obese, the hernia is not easily reduced, and he prefers to remain awake during the procedure. In still another patient inhalation anesthesia with cyclopropane may be better because he is uncooperative, has severe hypertension, has a hernia difficult to repair, and early awakening is preferred.

The essential elements in safe and satisfactory anesthesia for the elderly patient include not only intelligent choice of agent and technic with reference to the factors outlined, but also strict attention to the avoidance of excessive depression. In addition the anesthetist must be able with facility to eliminate the effects of the anesthetic, not only during the operation but in the immediate postanesthetic period. In respect to the avoidance of excessive depression, it should be remembered that standard doses and concentrations of drugs may be excessive for the elderly patient. The drugs should be applied in small doses and concentrations until the desired effect is produced in the particular patient being treated. It is much better to use small doses and low concentrations which may be repeated than to use standard or relatively larger doses which may cause unnecessary depression, difficult to reverse. One is frequently surprised to find that only relatively homeopathic doses are needed to provide suitable depression in the aged patient.

## THE POSTOPERATIVE PERIOD

During the immediate recovery period, frequent checks of blood pressure and pulse are necessary. Hypotension must be avoided, for this leads to irreversible shock and to intravascular thrombosis with the danger of pulmonary embolus. The patient should be mobilized as soon as possible following the surgery. Adequate help must be available to transfer the patient to a chair on the day of surgery and two or three times daily thereafter. If possible, a walk about the bed should be encouraged and aided. The patient must be turned frequently and encouraged to cough. Antibiotics are routinely given to help prevent infective pulmonary and peritoneal complications.

The principles described relative to the anesthesia also apply to the administration of sedative and analgesic drugs during the postoperative period. Nerve block at the time of completion of the operation, to prevent upper abdominal and thoracic pain, often is very helpful. The routine administration of drugs is entirely unwarranted and frequently is the source of serious postoperative complications such as atelectasis, ileus, and gastric dilatation. It is very important in the older patient that the doses of drugs be individualized and given on a single-order basis. It should be remembered that approximately 33 per cent of all postoperative patients require no analgesic drug of any kind, and it is especially unnecessary to provide routine "p.r.n." orders of depressant drugs in the older patient.

If a Levin tube has been put into the stomach, it is usually withdrawn at the first sign of peristalsis. The prolonged use of a naso-gastric tube leads to increased

mucus secretion and retention and often to atelectasis. Constant suction through a naso-gastric tube also leads to electrolyte deficiencies which, in the aged, are far more difficult to control or to correct than in a younger individual. For this reason, not infrequently two other methods are used for decompression. At the time of surgery a tube may be introduced through the stomach wall and guided into the small bowel. The site at which the tube emerges from the stomach is fixed to the abdominal wall and the tube is passed to the outside of the abdomen (7). According to another method, a tube may be led in a retrograde manner directly through the wall of the small bowel, the site of its emergence from the bowel being fixed to the peritoneum where the tube is brought through a small incision in the abdominal wall (8). In either instance adequate decompression can be accomplished by attaching the tube to a suction apparatus of the Wangensteen type. This avoids irritation of the nose and throat and the dangers of atelectasis. To establish a means of aspirating large amounts of gastrointestinal fluids in the aged patient, without simultaneously providing a means of returning those fluids, may inject an insurmountable problem in fluid and electrolyte balance if suction is used for many days. When prolonged suction is a possibility, a second tube is inserted into the small bowel distally in the form of a Witzel jejunostomy; the aspirate can then be reintroduced into the bowel as early as the second or third day.

During this period the most important problems concern fluid and electrolytes. It is our strong feeling that many elderly patients are killed by overzealous treatment during this interval (3). It is very rarely that an aged patient requires more than 2,000 ml. of fluid per day in addition to replacement of any aspirate from the gastrointestinal tract. This is not the time to attempt to build up the patient's nutritional state by overloading his circulation. The main object is to tide him over the early convalescent period so that he can begin to take foods and fluids orally. His body stores will be replenished much more satisfactorily by the oral route than by parenteral means. It is well to remember that in the immediate postoperative period the patient tends to retain sodium and chloride. It is unwise to give him salt during the first 24-hour period. In the second 24-hour period, usually only enough salt for replacement of aspirate is all that is required. If it is known that a patient will have a suction tube in place for a period longer than three days, it is wise also to begin administration of potassium, 2 grams daily in the parenteral fluids. The reckless administration of large quantities of fluids and salt will in many instances produce edema and this, in turn, will start a whole cycle of complications from which it may be impossible to extricate the patient. At all costs, overtreatment with parenteral fluids and salt must be avoided.

## SUMMARY

1. The principles of handling the aged surgical patient are discussed relative to preoperative, anesthetic and postoperative care.

2. An approach to therapy, based upon fundamental principles, will always be applicable to special problems. Therapy in the aged patient becomes less complex when approached in this manner.

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# THE IMPORTANCE OF ROUTINE ROENTGEN-RAY EXAMINATION OF THE CHEST IN PATIENTS OVER MIDDLE AGE

RICHARD H. SWEET, M.D.* AND EARLE W. WILKINS, JR., M.D.*

*Boston, Massachusetts*

During the past five years there has been an increasing awareness of the value of routine roentgen-ray examination of the chest. This method was employed originally as a means of case-finding for the detection and control of tuberculosis in the population at large, or to screen applicants for certain types of work such as food handling. It was soon discovered, whenever large groups of supposedly normal people were studied in this way, that in addition to pulmonary tuberculosis an appreciable number of cases of disorders of the heart and mediastinum and especially nontuberculous lesions of the lung were found. It soon became obvious that this procedure was valuable, not only in the field of public health but also as an aid in the management of the health problems of the individual patient.

Excluding from consideration all but the pulmonary cases, it is relatively simple to recognize the ordinary manifestations of tuberculosis or multiple metastatic malignant lesions. This leaves a group of cases of particular interest, when a single circumscribed shadow is discovered in the lung field. The differential diagnosis of such isolated shadows is of great importance to the individual patient from the standpoint of therapy. It has been learned from the study of various series of such cases that, although many of these shadows are due to benign inflammatory or neoplastic lesions, a large proportion of them turn out to be those of primary carcinoma of the lung, often in a relatively curable stage. The importance of finding a pulmonary carcinoma in its early phase of evolution, long before the patient would have been led to seek medical advice because of the occurrence of symptoms, is obvious. It is true also that the majority of primary carcinomata arising in the periphery of the lung, as opposed to those originating in a major bronchus, usually do not cause symptoms at an early stage. The presence of such asymptomatic lesions can only be known by roentgen-ray visualization.

As would be expected, most patients with carcinoma of the lung are beyond middle age. It is of interest, however, that some of the patients with nonmalignant lesions (including tuberculomas) are also in the older age group. Routine chest examinations are obviously important at all ages.

## ANALYSIS OF EXPERIENCE

During a five-year period ending in June 1953, 55 patients with single shadows in the lung, discovered on routine roentgen examination of the chest, were operated upon on the surgical service of the Massachusetts General Hospital. Table 1 gives the ages by decades of this group of patients. The age distribution is con-

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* Address: 205 Beacon Street.

TABLE 1. *Age distribution in 55 patients with isolated shadows in the lung*

| Ages by decades | No. of patients |
|---|---|
| 20–29 | 1 |
| 30–39 | 8 |
| 40–49 | 9 |
| 50–59 | 18 |
| 60–69 | 17 |
| 70–79 | 2 |
| *Total* | 55 |

TABLE 2. *Diagnosis established in 55 cases of isolated shadows in roentgen films of the lungs*

| | | |
|---|---|---|
| *Primary Malignant Neoplasms* | | 24 |
| Carcinoma | 20 | |
| Pulmonary alveolar adenomatosis | 2 | |
| Mesothelioma | 2 | |
| *Metastatic Malignant Neoplasms (single)* | | 5 |
| Renal-cell carcinoma | 2 | |
| Gastrointestinal tract carcinoma | 2 | |
| Other | 1 | |
| *Benign Neoplasms* | | 12 |
| Hamartoma | 6 | |
| Adenoma of bronchus | 2 | |
| Cyst | 2 | |
| Neurofibroma | 1 | |
| Thymoma (in the lung) | 1 | |
| *Tuberculosis* | | 12 |
| Tuberculoma | 9 | |
| Local pneumonitis | 3 | |
| *Miscellaneous* | | 2 |
| Fibrin body (?) | 1 | |
| Congenital malformation | 1 | |

sistent with that observed in the adult population of a large general hospital to which are sent many patients with special diagnostic problems. This may explain the fact that a relatively large number of the patients in the series were over 40 years of age (46 patients) and that 74 per cent were over 50 years of age (37 patients).

With these facts in mind, it is interesting to observe the relative occurrence of the several diseases which were proved to exist at operation. These are shown in Table 2. Thus of 55 cases, 29 were malignant tumors; and of these 24 (40 per cent) were primary in the lung. Of these 24 cases of primary neoplasm, 20 were bronchogenic carcinoma, the majority arising in the periphery of the lung. Many of these were small and apparently early enough to give a favorable prospect of long survival after removal. That such was the case is suggested by the data in Table 3, which lists the type of procedure carried out. Fourteen of the 20 patients were treated by lobectomy alone, not because they were poor risks for pneu-

TABLE 3. *Type of operation performed in 20 cases of primary carcinoma of the lung discovered in an early stage of the disease*

| | |
|---|---|
| Lobectomy | 14 |
| Pneumonectomy | 3 |
| Segmental excision | 1 |
| Biopsy | 1 |
| Drainage of malignant abscess | 1 |

TABLE 4. *Age distribution of patients with carcinoma of the lung*
(20 of 55 cases)

| Age by decade | Total No. in series | No. with carcinoma |
|---|---|---|
| 20–29 | 1 | 0 |
| 30–39 | 8 | 0 |
| 40–49 | 9 | 1 (11%) |
| 50–59 | 18 | 7 (38%) |
| 60–69 | 17 | 10 (58%) |
| 70–79 | 2 | 2 (100%) |

TABLE 5. *Age distribution of patients with tuberculoma or other single lesions due to tuberculosis*
(12 of 55 cases)

| Age by decades | Total No. in series | No. with lesion due to tuberculosis |
|---|---|---|
| 20–29 | 1 | 1 (100%) |
| 30–39 | 8 | 3 (37%) |
| 40–49 | 9 | 3 (33%) |
| 50–59 | 18 | 3 (17%) |
| 60–69 | 17 | 2 (12%) |
| 70–79 | 2 | 0 |

monectomy, but because in the majority of instances the growth was small and peripherally located. The importance of this observation is immediately apparent when it is realized that the majority of the patients who were found to have a primary carcinoma of the lung were old, or at least beyond middle age. As shown in Table 4 the relative occurrence of carcinoma of the lung among the 55 patients increased strikingly with each succeeding decade. In each of the 19 patients over 50 years of age the lesion was found to be primary carcinoma of the lung. This represents 38 per cent of the entire group of 55 subjects. It is of interest further that of the 5 patients whose pulmonary shadow was proved to be due to a single metastatic lesion, 3 were 50 years of age or older.

As would be expected, the occurrence of tuberculoma and other single lesions due to tuberculosis was principally in the younger decades, but it is significant from the point of view of the importance of the finding of isolated shadows in the lung in people beyond middle age, that 5 of the 12 cases of tuberculosis occurred among patients 50 years of age or older. These data are shown in Table 5.

## DISCUSSION

The analysis of a series of cases such as these serves to emphasize the importance of routine roentgen examination of the chest, particularly among patients in the older decades, because of the frequency in later life of the finding of an unsuspected primary pulmonary carcinoma. In addition, it is shown that other important lesions, such as tuberculomata and what appear to be single metastases from primary foci elsewhere in the body, may be discovered and dealt with in a satisfactory manner.

It is apparent from these observations that the clinician must adopt a routine policy with regard to the management of cases of unsuspected pulmonary lesions discovered by routine roentgen-ray examination of the chest. Because of the fact that it is rarely possible to establish a definite diagnosis on the basis of roentgen examination alone, and because of the fact that many of these lesions can be cured when found before clinical symptoms develop, it is imperative that (unless there is some physical contraindication) the benefit of surgical extirpation of the lesion should be offered to every patient in whom a silent pulmonary shadow is observed. In fact, the finding of an unsuspected pulmonary shadow such as those under consideration provides a unique opportunity, particularly among older patients, to cure what might become a hopeless lesion if allowed to go until symptoms develop. The fact that some of the cases will turn out to be benign should not be allowed to militate against the policy of exploration, because of the relatively slight risk of operation under these circumstances. In the series presented, though many of the patients were old, there was only 1 operative death. This occurred in a man 63 years of age who had long-standing chronic bronchiectasis of the lower lobe of each lung and the middle lobe on the right. A small carcinoma was discovered on the right side which could have been treated by lobectomy alone, if it had not been for extensive bronchiectasis in the middle and lower lobes, which made it necessary to perform a pneumonectomy. The respiratory reserve in the already partially crippled left lung was insufficient to maintain life. This is an example of one of the contraindications to surgery.

It is recommended, however, that exploratory thoracotomy should be advised in every instance when a single asymptomatic shadow is discovered in the lung, unless there are obvious contraindications. The contraindications which should be observed, subject to variations from case to case and the experience of the individual surgeon, are as follows:

1. *Excessive age.* This is a factor about which no arbitrary statement can be made. Obviously some elderly persons are better risks for surgery than many who are chronologically much younger.

2. *Severe cardiac disease.* It is striking to observe how rarely the heart is the cause of lethal complications after thoracic surgery, even in patients with known episodes of myocardial infarction in the past. Obvious decompensation is, however, a definite contraindication to surgery.

3. *Concurrent pulmonary disease.* Co-existing active pulmonary tuberculosis, old fibrotic disease (tuberculous or otherwise) extensive chronic bronchiectasis, or crippling pulmonary emphysema, when extensive enough to decrease the ventila-

tory capacity of the lungs below a safe level, are obvious contraindications to pulmonary surgery.

4. *Severe asthma.* It has been found that bronchial asthma of severe degree provides a serious risk for any kind of pulmonary or other intrathoracic operation. Surgery should not be advised for such patients unless the asthma can be overcome temporarily, as in some instances by the administration of cortisone.

As an illustration of the importance to the patient of the discovery of small symptomless pulmonary lesions, the following case histories are presented:

*Case 1.* B. P., a woman aged 68 years, was admitted to the Massachusetts General Hospital on January 3, 1950. She had had a number of previous admissions for various reasons, including coronary heart disease with bundle branch block. Palpitation and tachycardia had been present for ten years, and there had been occasional attacks of sharp substernal pain without radiation. Four months prior to this admission she had noticed the onset of persistent cough. There had been no hemoptysis or other respiratory symptoms, except that she had had more frequent colds than usual during the previous year. A roentgen examination of the chest (Fig. 1) on December 6, 1949 had showed a 2-centimeter lesion in the left upper chest, although previous films made at intervals of six months to observe the condition of her heart, had shown none.

Physical examination showed a soft blowing systolic murmur. The blood pressure was 180/90. Proctoscopy gave negative results. An intravenous pyelogram and gastrointestinal x-ray examination showed nothing abnormal. There was no blood in the stool by the guaiac test. The patient had had bilateral mastectomy for chronic cystic disease.

After preparation with a low-salt diet, the patient was operated upon on January 12, 1950. A left upper lobectomy was performed. In the anterior segment of the left upper lobe, almost in the center but not near the main bronchus, there was an irregularly shaped, small, firm tumor mass (Fig. 2). The hilar lymph nodes were small and anthracotic. No suggestion of metastatic areas could be found anywhere. The upper lobe

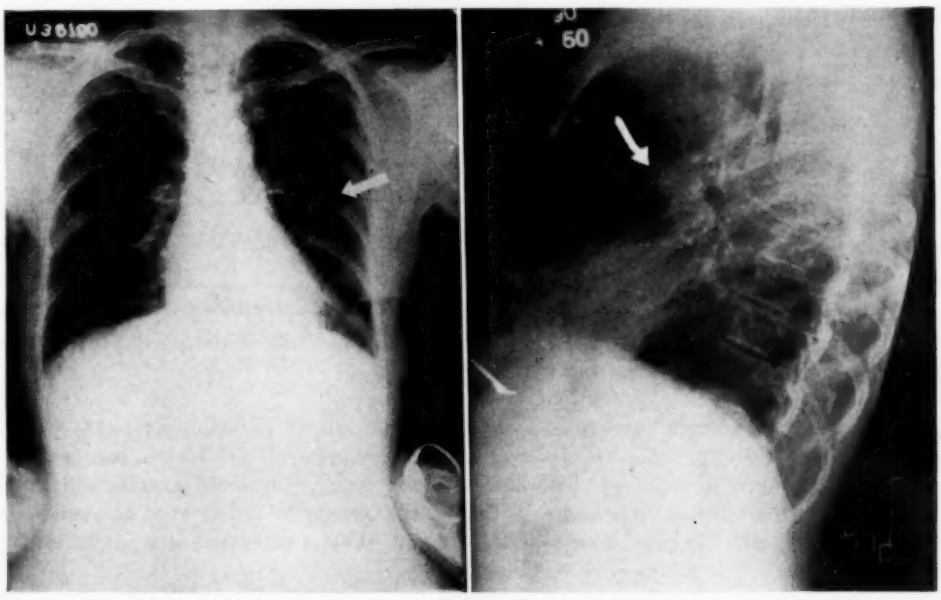

FIG. 1. Case 1. Reproduction of roentgen-ray film of the chest, showing bean-sized shadow in the anterior segment of left upper lobe.

was removed without difficulty. The lower lobe expanded well at the completion of the procedure.

The patient's postoperative convalescence was satisfactory and was marred by only one episode of paroxysmal tachycardia such as she had had at times preoperatively. This subsided overnight and she made an otherwise uneventful convalescence. The incision healed well. A postoperative roentgen examination of the chest showed good aeration of the remaining lobe of the left lung. She was discharged from the hospital on her eighteenth postoperative day. Her course since then has been followed with roentgen examinations at six-month intervals. She has remained well and free from evidence of recurrence.

FIG. 2. Case 1. Gross appearance of the lesion after left upper lobectomy

The operation listed in Table 3 as drainage of malignant abscess merits further description and thereby will exemplify the natural course of an asymptomatic pulmonary nodule not subjected to extirpation.

*Case 2.* J. A. N., a male aged 64, was first hospitalized at the Massachusetts General Hospital from May 21, 1947 to July 18, 1947, because of an ulcerating lesion in his stomach, thought to represent carcinoma. Accordingly, subtotal gastrectomy, splenectomy, partial pancreatectomy and resection of the transverse colon were necessary. The pathologic diagnosis, however, was gastric ulcer. A chest roentgenogram taken on May 26, 1947 during hospital admission, was clear.

He reported to the Out Patient Department on November 30, 1949 because a survey chest film had shown an abnormal density in the right mid-lung field. He had *no symp-*

*toms*. Hospital admission was advised but refused by the patient. He was not seen again until January 24, 1951, fourteen months later, when he reported to the Out Patient Department because of cough with blood-streaked sputum. This had first been noticed on January 22, 1951. A chest film at this time showed a large, lobulated density measuring 7.5 cm. in diameter and occupying the posterior segment of the right upper lobe. Hospital admission was again advised and again refused by the patient.

He was finally admitted to the hospital on December 26, 1952 because of pain added to his continuing hemoptysis. By x-ray examination there now existed an abscess, probably from broken-down tumor. Extirpation was out of the question. Aspiration biopsy failed to produce a diagnosis. The lesion had further increased in size. He was discharged on January 10, 1953.

The symptoms became increasingly severe and he was readmitted on March 21, 1953. Drainage was elected as a palliative course; when accomplished, this yielded a diagnosis of undifferentiated carcinoma of the lung. He was ultimately discharged on May 5, 1953 and was last seen in the follow-up clinic on May 28, 1953.

It is interesting to note that symptoms of this carcinoma did not appear until fourteen months after it had first been detected on roentgen examination. It is known from his previous films that it did not exist roentgenographically forty-four months before symptoms. It is presumed to have appeared first by x-ray detective means somewhere in the interval between forty-four and fourteen months before symptoms.

# GALLBLADDER SURGERY IN PATIENTS OF THE OLDER AGE GROUP

ROBERT M. ZOLLINGER, M.D.* AND HOWARD D. SIRAK, M.D.**

*The Department of Surgery, the College of Medicine, and the Surgical Service, The Medical Center, Ohio State University, Columbus, Ohio*

Patients in the older age groups who are suffering from gallbladder disease require additional measures in order to make their surgical treatment more satisfactory. These measures are first concerned with the accurate selection of cases for surgery, utilizing methods which establish a diagnosis by positive means as well as by exclusion of pathology elsewhere. In addition, special attention must be paid to the details of management during the preoperative and postoperative periods as well as during the operation itself (1). The following is an account of the methods employed during the past six years in the surgical treatment of 571 patients with gallbladder disease. Three hundred and twelve (55 per cent) were over 50 years of age, of whom 152 (approximately half) were 60 years of age or over.

## PREOPERATIVE MANAGEMENT

Although such patients usually do not present a special problem, a significant number of them who consult their doctor for treatment of gallbladder distress have co-existing disease in other organs. Indeed, the cause of a patient's complaints actually may be a lesion which is mimicking gallbladder disease. This is not surprising when one considers the sharp rise in the incidence of neoplastic and degenerative disease in the population over 50 years of age. Therefore, because of the possible presence of a lesion which otherwise might remain hidden, a policy of thorough evaluation is routinely applied to all patients past the age of 50, no matter how typical the history or how definite the physical findings supporting gallbladder disease seem to be. This is aimed at further improving the results and reputation of the surgical treatment of gallbladder disease and at dispelling the notion, held by some patients, that even after operation they might not be relieved of their complaints. Such a change in attitude would encourage patients to seek consultation earlier, rather than to wait for a recurring attack or complication to develop in later years when the risk would be increased.

The opportunity (and obligation) to accomplish such improvement is greatest in cases of chronic gallbladder disease. A definite diagnosis can be reached only after a careful analysis of the clinical features, supported by adequate roentgenologic studies of gallbladder function. A single non-visualizing cholecystogram should be repeated after excluding the presence of other conditions, such as jaundice or severe liver disease, which prevent the proper absorption of the dye.

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* Professor and Chairman of the Dept. of Surgery.

** Instructor and Chief Resident.

It is also important to be sure that the patient has ingested the proper number of dye tablets or that he has not vomited them. In interpreting cholecystograms, no particular significance should be attached to unusual gallbladder sizes and shapes or to varying densities of filling. The presence of a repeatedly non-visualizing gallbladder, particularly if calculi are also seen, supported by a consistent history, establishes a firm diagnosis of gallbladder disease. A patient having the diagnosis proved in this manner can be assured of a good result, thereby justifying the minimal operative risk.

Nevertheless, despite a proved diagnosis of gallbladder disease, in older patients it is necessary to search for a lesion elsewhere in the gastrointestinal tract which might be causing the patient's complaints. Complete barium studies (a proctosigmoidoscopic examination is also included) are mandatory, because they may disclose the presence of a hiatus hernia, duodenal ulcer, or gastrointestinal carcinoma, which on further analysis will prove to be a source of a patient's complaints. During the same period in which this series of gallbladder cases was being treated, there were several patients referred for cholecystectomy who, on further study, were found to have a carcinoma of the colon in the area of the hepatic flexure.

If a duodenal ulcer is present along with gallbladder disease, cholecystectomy should be urged, so that the patient will be better able to tolerate an ulcer regimen. In like manner, patients with cholelithiasis who suffer from recurrent attacks of pancreatitis should be suspected of having a common-duct stone. In such instances, removal of the gallbladder and exploration of the common duct are indicated.

Coronary artery disease (proved or suspected) is not a deterrent to surgery. The distress of angina is easily confused with, or may even be aggravated by cholecystitis. Indeed, many patients have been gratified to find themselves relieved of their anginal symptoms after cholecystectomy. A careful study of the heart is required in any patient before surgery, but obviously the more elderly require a more thorough investigation, which should include an electrocardiogram and perhaps the two-step exercise test in addition to the customary chest roentgenogram and blood pressure determination (2).

The vital capacity determination is a useful means of assessing pulmonary function and the patient's fitness in general. This is a gross method and no exact prognostic data can be derived from its values. This test is easily made by means of a small, portable spirometer. By keeping a daily record, one obtains an index of the progress of an elderly patient's vigor and vitality in response to treatment. The more the condition of the patient improves, the greater his vital capacity becomes. Elective surgery will be better tolerated if the vital capacity reaches 2,000 cc. or more. Not infrequently this requires specific therapy to the respiratory tract itself. Many of these patients are heavy smokers and have a productive smoker's cough, a fact which routine questioning and chest roentgenograms will usually fail to disclose. Priestley (3) has recently emphasized the importance of specifically asking the patient to cough in order to detect the presence of secretions accumulated in the airways. Steps must then be taken to remove this excessive mucus, to prevent postoperative pulmonary complica-

tions. In order to reduce the irritation to the respiratory passages, all patients are urged to stop smoking (or at least drastically curtail it) during the preoperative period. Dental hygiene is also important: prophylactic cleansing and care of infected teeth will help prevent pulmonary infection.

A valuable adjunct to preoperative therapy is the blood volume determination, particularly in elderly patients with weight loss, and especially if they are jaundiced. We have observed in a number of such patients that for every pound of weight lost, there is an approximate 1 per cent decrease in the plasma volume. The routine red blood cell count, hemoglobin and serum total protein determinations usually fail to disclose these alterations, inasmuch as they are unable to measure the total circulating blood volume. This is not satisfactory for the treatment of older patients, because many of them coming to surgery have a large deficiency in blood volume. Consequently, an adequate number of transfusions should be given during the preoperative period, to help put the patient in optimum condition for operation. Only by calculating deficits in the total blood volume, plasma volume, total circulating protein and red cell mass can accurate replacement be accomplished (4). In the absence of jaundice, the Evans Blue dye method (T-1824) is satisfactory; however, if jaundice is present, the radioactive iodinated human serum albumin technique should be employed for accurate results.

Although considerable stress has been placed on the value of this type of therapy, some physicians are reluctant to employ it in the more elderly patients for fear of overburdening the circulation. This attitude is probably no longer justifiable. If preoperative blood transfusions for purposes of restoring depleted blood volume are limited to 500 cc. per day, there is little likelihood of embarrassing the circulation. Furthermore, as Elman (5) has pointed out, the benefits derived from this measure greatly outweigh in importance the possible risks associated with its use. Experience has shown that the patients with a decreased circulating protein level are the ones who are most likely to go into shock during the operation, whose wounds heal most poorly, and who have the most postoperative complications.

Closely allied to the status of the blood volume is the condition of the patient's nutrition. This problem has two diametrically opposite aspects, which have an important bearing on the welfare of the patient. On the one hand, there is the problem of the depleted patient (for example, one with jaundice from a common-duct stone) and on the other, the obese patient. In the former, the aim is to provide enough calories to return the patient to a weight-gaining trend. This must be undertaken in a manner which provides a large daily intake of protein (125–150 Gm.), carbohydrate and vitamins, especially vitamin C (1 Gm.), while restricting fat. Getting the patient to consume this required amount of food may be facilitated by individualizing the diet as much as possible, so that it caters to the patient's taste. However, it may be necessary to pass a small polyethylene catheter into the stomach for forced feeding. A mixture of homogenized milk fortified with protolysate (50 Gm.) and Dexin (50 Gm.) may be used for this purpose. In patients who have obstruction of the bile duct, the addition to the milk mixture of 1 Gm. of Sorlate (Tween 80) or bile 'borrowed' from T-tube

drainage of other patients, will bring fat absorption back to normal and increase the total caloric intake. One should not hesitate to utilize this method when it is indicated, because the increased safety of operating on older patients who show a weight-gaining trend justifies an unrelenting effort to restore their nutritional balance.

Elective surgery in the patient who is markedly overweight should be deferred, if feasible, until adequate weight reduction is accomplished. This is an important measure which does not usually receive the attention it deserves. Especially in the older patients, in whom the incidence of complicated cases is higher, gallbladder surgery can be hazardous. Therefore, it behooves the surgeon to have the patient in the optimum condition to facilitate the operation. The weight reduction program is more easily accomplished during the preoperative period, when the patient's cooperation is spurred by fear of provoking an attack from injudicious eating. A diet of around 1,000 calories is sufficient.

In most patients with gallbladder disease the urinary tract offers little difficulty, except in the very aged. In these cases it may be necessary to supplement the usual laboratory tests with an intravenous pyelogram, in order to get more detailed information on kidney structure or function. However, of more general application is the desirability of teaching the older male patients to practice using a urinal in bed prior to operation, so that they will not be faced with this problem for the first time during the early postoperative period. This will make voiding easier and do away with the unpleasantness and possible complications from catheterization. If actual prostatic obstruction is present, urologic consultation is required. A transurethral resection may be indicated.

All the benefits of the foregoing thorough preoperative evaluation will be compromised if it is not supplemented by efforts to dispel the gloomy defeatist attitude which so many of these chronically ill patients exhibit. Assurance and personal attention will go a long way towards restoring the patient's confidence and gaining his cooperation.

*Acute cholecystitis.* Unlike patients with chronic gallbladder disease, in whom there is time to assess completely the other organ systems, the patient with acute cholecystitis receives a type of management which is, of necessity, more concentrated on the study and control of the biliary tract pathology itself. This complication was encountered 46 times in the 312 patients over 50 years of age—an incidence of 15 per cent. A similar incidence was found in 259 patients under the age of 50. In 7 patients of the older group, the situation was deemed so precarious that cholecystostomy was performed (6). This operation was not used in any of the younger patients. Interestingly enough, there was no fatality in the older group, but there was 1 in the younger patients. The following is a description of the methods used in managing patients with this complication.

These patients should be hospitalized immediately. A flatplate and upright film of the abdomen, and a chest roentgenogram are obtained to aid in establishing the diagnosis (perhaps by the visualization of stones in the gallbladder) and to exclude the presence of some other intra-abdominal and intrathoracic disease. The patients receive small doses of Demerol and atropine, constant gastric suction

for vomiting, and intravenous fluids to combat dehydration. Antibiotics may be used; however, the inflammatory process is usually on a chemical rather than an infectious basis. An evaluation of the patient's general condition by means of abdominal signs, pulse, temperature, and white blood cell count every four hours, is necessary in order to select properly the cases which will require urgent surgery. If, after an interval of several hours, a good response is obtained with this management, as shown by diminution of pain and improvement in the vital signs, conservative management is in order for a few days until the acute phase has subsided; then the operation is carried out. If, on the other hand, the white blood cell count rises and the disease process shows signs of progressing in spite of adequate hydration, bed rest and sedation, then surgery must be undertaken day or night without further delay. A word of warning is needed here. In appraising signs and symptoms of intra-abdominal disease in the more elderly patient, one must remember that these manifestations are frequently subdued and lack the clear-cut features found in younger people. The physician must not allow himself to be deceived, lest he fail to recognize the fact that the disease is progressing and that perforation is becoming imminent. Since acute pancreatitis can easily be confused with acute cholecystitis, and in rare instances accompanies it, a serum amylase determination is routinely obtained in all these patients. The presence of acute pancreatitis precludes operative intervention until it has subsided, except in those cases in which it is associated with a progression of the acute cholecystitis.

*Jaundice.* Finally, mention must be made of those occasional patients who are jaundiced. A differential diagnosis must be made between jaundice due to common-duct stone and that due to some other cause such as carcinoma of the head of the pancreas, or, of more importance, to hepatitis. In a recent analysis of 100 consecutive cases of jaundice submitted to surgery on the surgical services, 89 cases were of the obstructive type and 11 were due to medical causes (7). Of these 89 patients whose condition was correctly diagnosed as 'surgical jaundice' preoperatively, in approximately half, or 48, the jaundice was due to common duct stone. Benign stricture accounted for 7 and carcinoma for the remaining 34. It is believed that a further reduction in the number of patients with a 'medical type' of jaundice uncorrectly operated upon can be achieved by a more thorough clinical analysis and by taking time to repeat laboratory tests which yield equivocal or abnormal results.

In a patient who is jaundiced, the diagnosis of common-duct stone should be suggested by a history of prominent nausea and vomiting, colic, chills and fever, or recurrent jaundice. Clay-colored stools coincident with the bout of jaundice may occasionally be present. Of considerable help is a group of laboratory tests which should be used to support the clinical findings.

An elevated serum alkaline phosphatase level provides the best evidence of extrahepatic obstruction; the prothrombin time (and perhaps the percentage of cholesterol esters) is a good test for uncovering functional impairment; and cephalin flocculation and thymol turbidity help to determine the amount of cellular destruction. The Van den Bergh test, like the icterus index, is useful only for following the progress of the jaundice.

If patients with an equivocal history and physical examination show laboratory data indicating an impairment of liver function or cellular damage, then the surgeon must be very wary of operative intervention.

## THE OPERATION

A Levine tube is routinely passed into the stomach before surgery, and the stomach contents aspirated. Generally, the anesthetic chosen should be one with which the anesthetist has had the most experience. A light inhalation anesthetic with sufficient curare (or curare-like drug) to produce adequate muscular relaxation has been found satisfactory for most cases. Whenever a general anesthetic is used, endotracheal intubation is employed because it permits complete control of the respirations at all times. Its presence facilitates the introduction of a high concentration of oxygen and the frequent aspiration of mucus from the tracheobronchial tree. In very poor-risk or aged patients, as might be encountered in cases of acute cholecystitis, intercostal block supplemented with 1 per cent procaine (without epinephrine) infiltration of the skin and the abdominal wall at the incision site is indicated (8). A right paramedian incision is our choice in the majority of instances, particularly if it is expected that the common duct will be explored. In the markedly obese patient or in those patients in whom a distended gallbladder is palpated lying far out laterally, a subcostal incision has been used to advantage.

Gentleness is of paramount importance in operating on patients in the older age groups. A sudden drop in blood pressure must be prevented by keeping bleeding at a minimum and avoiding the production of vasodepressor stimuli from strong traction on the mesentery. If a regional block or a very light general anesthetic is being used, a blood pressure drop due to vasodepressor stimuli may result from passing the hand against the under surface of the diaphragm while delivering downward the right lobe of the liver. Therefore, if it does not appreciably hinder the operation, this maneuver should be omitted.

The need for exploring the common duct will increase with the age of the patient. Glenn has suggested that patients over 60 who have a prolonged history of biliary tract disease constitute an indication for common-duct exploration (9). This is in keeping with our experience, as shown by comparison of 312 patients over 50 years of age with 259 patients under the age of 50. In the former group, duct exploration was performed in 47 per cent of the patients, and in the latter, in 39 per cent. However, stones were recovered in 43 per cent of the older group—a rate nearly twice as great as that in the younger group, in which it was 25 per cent. The total incidence of stones in each group was 25 per cent for the former and 10 per cent for the latter, respectively. The low rate of recovery of stones in these younger patients would suggest that the indication for exploration in some of the cases was too liberal. In defense of this attitude, it must be stated that this trend usually has been prompted by the many instances of retained common-duct stones encountered in patients returning dissatisfied with their previous gallbladder operation. On the other hand, however, this freer policy does seem warranted for the older patients, since it is substantiated by the higher incidence of common-duct stones in this series. In the individual case, the

decision to explore the common duct will be influenced by the presence of enlargement, the existence of small stones capable of passing through the cystic duct, and a history of colic, severe bouts of nausea or vomiting, chills and fever, or jaundice. Evidence of pancreatitis is another indication for exploring the common duct. In some instances cholecystostomy is all that is indicated, particularly if there is a difficult technical situation or if the patient's condition warrants a more minor procedure.

At the conclusion of the operation, an empty soft-rubber drain is placed in the foramen of Winslow. This drain and the T-tube are brought out through a separate stab wound lateral to the operative incision. Each should be separately fastened to the skin with a silk suture. The anesthetist may block the appropriate intercostal nerves with a long-acting anesthetic agent, to reduce incisional pain and thereby decrease postoperative narcotic requirements.

## POSTOPERATIVE MANAGEMENT

All patients in the older age group should be given intranasal oxygen during the recovery period. It is imperative that a competent person be in attendance to keep close observation on the patient's airway. Removal of mucus by catheter suction at frequent intervals will be necessary until the patient is fully awake.

The quantity of intravenous fluid given on the day of surgery and on the subsequent two or three days should be limited to approximately 2,000 cc. One liter should be given in the early morning, and another should be started in the afternoon. By distributing the fluid in this manner, the burden on the circulation is lessened, the patient's normal intake habits are more closely simulated, and the interval between infusions can be utilized to get the patient out of bed. An accurate record of the intake and output must be kept. In those individuals who have lapses of incontinence, or if maximum accuracy is desirable, an indwelling urethral catheter must be used.

All infusions should be given intravenously in the form of 5 or 10 per cent dextrose in water. Saline should not be given during the first forty-eight hours postoperatively, because it has been shown that the kidneys are unable to excrete it during this period. Furthermore, salt should be restricted in the aged, in order to avoid embarrassing the circulation and to prevent collection of fluid in the tissues. Moreover, these patients have a negligible salt loss, so that replacement is not required. Starting on the second postoperative day, if the urinary output has been adequate, 2 to 3 grams of potassium chloride should be added to one of the liters of fluid. This is the average maintenance dose and aids the return of normal intestinal function and recovery in general. Usually, by the second or third day, the patient is taking water and clear liquids orally. If the patient is tolerating oral fluids well, he is encouraged to drink as much of his daily requirement as possible, so that the infusions may be discontinued. The patient's oral intake is re-evaluated every afternoon, and if it appears that he will not meet his requirements, a supplementary quantity may be given intravenously.

Fluids should not be given by hypodermoclysis. The possibility of overloading the circulation is far outweighed by the hazard of clysis, which has been shown to

result in a serious alteration in electrolyte and water equilibrium when solutions of glucose (and other nonelectrolyte solutions) are used. Such a reaction causes a reduction in the circulatory volume which may, in turn, produce circulatory collapse with its dangerous sequelae, oliguria or anuria. Hyaluronidase preparations accentuate this harmful effect (10).

Constant effort is required to prevent thrombophlebitis during the postoperative period. An important factor in prevention is good preoperative preparation, which increases the patient's activity and restores his nutritional status. But because thrombophlebitis is especially apt to occur in patients in the older age group, a careful vigilance must be kept in order to detect its presence as soon as it appears. Inasmuch as the prophylactic employment of anticoagulant therapy is not practical, it is necessary to rely on a combination of measures to keep the incidence of this complication to a minimum. The insistence by the nursing and medical staffs that the patient exercise his lower extremities while lying in bed and the employment of early ambulation are helpful. Elastic stockings[1], if snug fitting, will compress the superficial venous circulation so that blood flow is increased in the deep venous system of the lower extremities, where a large percentage of thrombi originate. However, these stockings should not be used in individuals whose arterial circulation in the lower extremities is compromised (11).

The Levine tube is customarily removed in twenty-four hours, to relieve irritation and accumulation of secretions in the hypopharynx. The rubber drain is advanced, starting on the second postoperative day, and is taken out by the third day, unless there is bile drainage. The presence of a drain is often painful, and it should be removed as soon as it has fulfilled its purpose. The T-tube is drained into a dependent container. A convenient method is one in which the tube empties into a rubber glove which is carried dependently in a pocket; after about seven days, the rubber glove may be placed in an upper pocket so that its elevated position will cause the bile to flow out of the papilla. If this does not cause discomfort to the patient, then there is good evidence that swelling around the papilla has subsided, so that the T-tube may be safely removed around the seventh or eighth day. In most instances, a cholangiogram is obtained, in which case the removal of the tube is delayed an additional day in order to maintain common-duct drainage should pancreatitis happen to develop from the procedure.

## DISCUSSION

The mortality in patients of the older group was 2.6 per cent and in the younger patients it was 1.1 per cent. An unusual finding was that there was 1 death among the younger patients with acute cholecystitis, but no deaths from this complication in the older group. Of the 8 deaths occurring in the 312 patients over 50 years of age, 4 were due to acute pancreatitis developing during the postoperative period. In each of these the common duct was explored. Two patients were

[1] Obtained from Bauer and Black in large, medium and small sizes. Two types are available: one which goes above the knee, and another which reaches to the knee. The latter is preferable, because it will not roll up.

50 years old, one was 64, and the other 74. No definite reason can be given for this high incidence; however, it appears related to the greater number of common-duct explorations and the higher incidence of stones in persons over 50. If it were not for the unusual prominence of this complication in the older group, which accounted for half of the deaths, the mortality figures would be about the same for both age groups. Among the remaining fatalities, liver disease (associated cirrhosis or hepatitis) caused the death of 2 patients, one aged 53 and the other aged 61. These deaths were preventable, inasmuch as the presence of liver disease was known preoperatively, but the severe distress produced by the gallbladder disease prompted the surgeon to proceed with the operation even though he appreciated its possible dire consequences. The other 2 fatalities were caused by cerebral thrombosis occurring in a patient who was 64 years old, and by cardiac arrest in one who was 56 years old.

It is notable that none of the 312 older patients died of those conditions which are commonly responsible for most of the mortality in this age group. Deaths from the anticipated cardiac, pulmonary and renal complications were conspicuously absent. It is believed that this may be attributed to the program established for the care of these older individuals, which places considerable emphasis on attending to the details of management. This regimen is devised especially for the complicated cases, in order to compensate for a situation which in many instances could have been prevented had the patient undergone surgical treatment earlier. Such a program sorely taxes the medical and hospital personnel. Therefore, it would be more practical and safer to attempt to decrease the number of these complicated cases by having patients consult the surgeon when the gallbladder disease is in a more benign form. The physician should bear this in mind when faced with the problem of advising younger patients with cholecystitis to undergo surgery. On the other hand, the advantages of having patients submit to operation sooner can be fully exploited only if the methods and results of surgical treatment of patients with gallbladder disease continue to improve. For older individuals this requires special considerations in order to avoid the many possible pitfalls. First, it is necessary to make sure of the diagnosis by excluding the presence of some other lesion simulating gallbladder disease, and then to be thorough in evaluating and preparing the complicated cases for surgery. In the case of the patient with acute gallbladder disease, close following of the white blood cell count, temperature and pulse is imperative; and for the jaundiced patient, special preoperative attention to nutrition and blood volume and prothrombin levels. Also to be included are prior assessments of the heart, lungs and kidneys, in order to forestall catastrophe during the postoperative period, and the selection of the proper operation to fit the needs of the individual patient.

In other words, the surgeon must be thorough throughout all phases of treatment, in order to obtain the consistently good results so sorely needed to dispel the prevailing fear and distrust of surgical treatment for this condition. Perhaps in this way the pernicious practice of deferring operation will some day be abolished.

SUMMARY

1. The details of the surgical management of 312 patients over 50 years of age with gallbladder disease are presented. One hundred and fifty-two, or approximately half of the patients, were 60 years of age or older.

2. Among those patients in the over-50 group who underwent common-duct exploration, stones were recovered in 43 per cent. The overall incidence of common-duct stone in the entire group was 21 per cent.

3. Acute cholecystitis was encountered in 15 per cent of the total number of cases. There were 46 patients with this complication, but there were no fatalities.

4. The mortality rate for the 312 patients over 50 years of age was 2.6 per cent. This was slightly more than twice the mortality rate (1.1 per cent) for a comparable series of 259 patients under 50 years of age. A comparison of these figures suggests the advantages of advocating operation at an earlier age instead of deferring surgical treatment until a complication develops.

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# RESTITUTIVE SURGERY OF THE HIP JOINT. ITS EVOLUTION TO THE PRESENT*

STEPHEN S. HUDACK, M.D. AND ROBERT F. COOKE, M.D.

*The Surgical Division, Saint Luke's Hospital, Cleveland, Ohio*

In the evaluation of a new approach to an old problem, it is well to examine the methods being superseded. It is important, also, to understand the perspective of the surgeons applying these methods. Most surgeons responsible for departure from established or old methods, if they have pride in their work, cannot refrain from comparing the new procedure with what has gone before, when stating what they may hope to accomplish with the new method. For this reason, we have sought to divide the consideration of the restitution of the injured hip joint into periods. These periods roughly coincide with the methods and the philosophies of the surgeons concerned. They have no relationship in time because, as we all know, there are progressive and conservative thinkers in surgery. The community, too, has its influence and what may still be conservative accepted practice in one area may, at the same time, be superseded in another area. Thus, in a sense, it is possible to trace the evolution of method and thought, as it has bearing on the problem being considered. Usually a method can be linked with a name, but original authorship of an idea is not always easy to pin down. The early period which we may call "Sandbags and death," is typified by Astley Cooper—not that he was responsible in any way for the deplorable philosophy of his time; he merely reflected it. The next period, earmarked by plaster fixation in abduction, may be called "The effective covering period." It represented some departure from the older philosophy of neglect and hopelessness but only obscured, and did not treat successfully the basic problem. This method may be associated with the name of Royal Whitman. Its influence was surpassed by that of the internal fixation period. (It is of interest to examine what Whitman thought of the period ahead of him and of the methods displacing his. This we shall do later.) The pin fixation period can be linked with Smith-Peterson, Moore, Johansson and others. Smith-Peterson's influence became dominant in this country and gave rise to some methods (*e.g.*, cups) which dealt with somewhat different aspects of the same problem. In between, and overlapping both the plaster and the pin philosophies, was the traction-suspension period. The writings of Robert Jones reflect the untrustworthiness of this method. Let us consider some of these methods and philosophies for background.

## SANDBAGS AND DEATH

This period actually extends back into antiquity but, for our purpose, it may be considered to cover from the time of Astley Cooper to the time of Robert

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Jones. It is difficult for us to comprehend the hopelessness and futility of the treatment of hip injuries in their time. Envisage the torture, both physical and mental, for an elderly patient who had broken a hip. To the pain and shock of injury was added the imprisonment and immobility produced by sandbags "supporting" the injured extremity. Imagine the futility reflected in the attitude of the doctor and the hopelessness of the immediate relatives. Even with good care, there was the great difficulty of fulfilling bodily needs and personal hygiene. Thus an attrition between vitality and immobility went on until one or the other conquered, and either the spirit or the corpus remained. There was either residual invalidism or release through death. It was from the dissecting table that Cooper contributed much to the understanding of fractures of the femoral neck.

Astley Cooper (1), writing on intracapsular fractures of the femur in 1842, said:

"I have now been thirty-nine years connected with St. Thomas's and Guy's Hospitals and for thirty-five years have enjoyed no inconsiderable share of the surgical practice of London. In the two hospitals.... adding to these, one case only in each year in my private practice.... they will collectively amount to two hundred and twenty-five cases. But dissections which I made early in life and opportunities I have since had of confirming these observations, have convinced me that fractures of the neck of the thigh bone generally unite by ligament and not by bone. In the examinations which I have made of transverse fractures of the cervix femoris, entirely within the capsular ligament, I have not met with one in which bony union had taken place, or which did not admit motion of one bone upon the other.

Baffled in our various attempts at curing these cases and finding the life of the patient occasionally sacrificed under the trials made to unite them, I should, if I sustained this accident in my own person, direct that a pillow should be placed under the limb throughout its length; that another should be rolled up under the knee, and that the limb should be thus extended until the inflammation and pain had subsided. I should then daily rise and sit in a high chair, in order to prevent a degree of flexion, which would be painful; and, walking with crutches, bear gently on the foot at first; then, gradually more and more, until the ligament became thickened, and muscles increased in their power. A high heeled shoe should be next employed, by which the halt would be diminished. Our hospital patients, treated after this manner, are allowed in a few weeks to walk with crutches, and in a few months they are able to use the limb without any adventitious support."

Cooper was an able and considerate surgeon, who treated the patient and not the bone lesion alone. He enjoyed a considerable and deserved repute, and scorned the bone setters of his time as charlatans.

But this gloom of futility was pierced by the light of courageous spirits. To help you understand what happened to the aged, let me cite for you what happened to the young in those times. John Coyle, a 21-year-old native of Philadelphia, seaman 1st class aboard the "Topaz," was reported by Captain Schuyler to be injured. On March 17, 1825, he had fallen from a hatchway upon the end of a barrel. He was abed for eighteen days aboard, was transferred to Porto Cavello Hospital, and then admitted in October to the Pennsylvania Hospital. He was seen by one of the distinguished surgeons of Philadelphia, and traction was applied to the injured area. He then went to the care of other colleagues. About a year later he was seen again, still in the hospital, by the original surgeon who

found him with a fixed adduction deformity. "This led to much reflection." I should like to quote further from Barton's report of the case (2):

"Accordingly on the 22nd day of November, 1826, assisted by Drs. Hewson and Parrish, I proceeded to do the operation publicly in the Pennsylvania Hospital. To a large medical class, and many respectable physicians assembled, I again represented the nature of the case, and of the operation and the views and course of reasoning which induced me to adopt it; stating, likewise, that I wished it to be distinctly understood, that a submission to my contemplated plans had not been urged upon my patient by any false or delusory promises; but that an explanation of his existing condition, and of the means proposed to be attempted for his relief, were fully made to him, in language adapted to his right comprehension of the matter, as well by my colleagues, as by myself; and that he authorized me thus publicly to state, that he was prepared to assume all and the exclusive responsibility for the issue. With this exculpation, therefore, the operation, as already detailed, was put into effect. The integuments and fascia being divided and raised, the muscles in contact with the bone, around part of the great trochanter, were carefully detached, and a passage thereby made, just large enough to admit of the insinuation of my fore-fingers, before and behind the bone, the tips of which met around the lower part of the cervix of the femur, a little above its root. The saw was readily applied; not one blood vessel required to be secured. The operation, though severe, was not of long duration, it being accomplished in the space of about 7 minutes".

Thus J. Rhea Barton, an honest surgeon even in those days, courageous but intimidated by preceding usage, let the sailor patient assume full responsibility. This happened one hundred and twenty-six years ago, in one of our best American hospitals. Imagine what must have happened in outlying communities. The sandbag era, to which Barton initiated the rebellion in America, may be summarized by quoting the reminiscence of the late William Darrach on morbidity and mortality in hip surgery preceding his time. "The exception was invalidism for the remaining years, the expectation was death."

Perhaps some comprehension of the philosophy of the sandbag period may be gained from Sir Arthur Keith's (3) writing about Hugh Owen Thomas:

"Thomas was the first to apply rigidly and completely the principle of rest as a logical system to such conditions and to carry it out in the form of enforced uninterrupted and prolonged rest. In case of fracture of the femur, in order that the patient might escape the disturbance caused by the act of defecation, he placed the bowel at rest by sedatives and low diet but never succeeded in keeping it still, beyond the twenty-first day. There is all the difference in the world between pious enunciation of a principle and its strict systematic and complete application. Therein lies the difference between Thomas and his predecessors" (concerning the philosophy of prolonged rest).

## EFFECTIVE COVERING (ABDUCTION)

The philosophy of rest carried over into the Whitman plaster-fixation period. Whitman (3), looking backward, wrote as follows:

"The typical chapters on fracture of the neck of the femur in textbooks have varied but little in succeeding generations. Much space is given to descriptions of specimens, manifestly atypical since they represent fatality, and differential diagnosis of the type of fracture to which treatment is to be adapted. The main purpose, however, seems to be to present all the obstacles to success, physical, nutritive and mechanical in order to up-

hold treatment of a quality that would not be tolerated for any other fracture, and to explain failure on other grounds than lack of opportunity for repair". He goes on to say that "Treatment conducted in accord with this teaching has been naturally of a most perfunctory character, indeed. It is stated in a recent paper that of 120 consecutive cases of ununited fracture at the hip, examined at the Mayo Clinic, not one had received efficient treatment at the time of the injury."

Efficient treatment of course implied the abduction plaster-spica method, which we call effective covering. Whitman cited statistics to the effect that in 55 per cent or more of cases, bony union was obtained. We know that this percentage ignored both mortality and morbidity. It ignored also the frequent ineffectiveness of closed reduction, as is now known since open reduction of the femur has been extensively practiced. Moreover, it did not take into account vascular injury and interposition. The follow-up periods hardly ever were long enough to uncover the aseptic necrosis and the painful degenerative changes which occurred later. So much for the backward glance by Whitman. Looking forward, he wrote about pinning operations (5):

"At the present time, the tendency is to encourage early movement in the treatment of fractures in order to improve nutrition and assure mobility. This is not practicable in the treatment of fracture of the neck of the femur, since it would prevent union in the transcervical type and might stimulate excessive callus formation about a fracture at the base of the neck and thus limit range of motion. The introduction of nails, screws or bone pegs is contraindicated, because they are unnecessary if the abduction method is properly applied, because they damage the cancellous tissue on which repair depends and because, in the event of the not unusual absorption of a part of the neck, the fragments would be actually held apart by the means intended to assure apposition."

Apparently there was a failure on his part to accede gracefully to what were then more progressive methods, advanced by Smith-Peterson and others. Smith-Peterson, in turn, in looking forward to articular replacement, had some sad things to say about it.

## TRACTION-SUSPENSION

Another influence was the method of traction-suspension, which reflected a dissatisfaction with the eight to twelve weeks of plaster immobilization. It was an attempt to limit the degree of fixation only to the amount necessary to accomplish repair—a sort of dynamic frustration philosophy.

Robert Jones (6) wrote in 1921:

"Elderly subjects must not remain in bed for more than the minimum period—perhaps only a week or so; the treatment should quickly be made ambulatory; The reason for this is not fear of pneumonia, but the risk of "moral", so to speak, or of the desire to help themselves be about again. . . . The union of a fracture of the neck of the femur in elderly subjects is generally considered to take place by fibrous and not osseous tissue, but the final result is much more often a pseudoarthrosis or false joint at the site of fracture; in spite of this, however, the functional result is good if the ambulatory weight relieving splint is worn from six to twelve months, the leg showing no sign of progressive shortening after the appliance has been discarded. . . . When no initial shortening exists, especially in transverse fractures, it might be desired to get the patient up and about early in plaster of paris spica, but the objections to this method are its tediousness in

case of adults and difficulty of combining traction or of utilizing physio therapeutic treatment. . . . As regards open operative treatment, it has at times been not unusual to endeavour to fix the head of the femur by one or more long screws driven through the trochanter, but the method is now almost universally discarded on account of the difficulty of uniting fragments in perfect position."

## ARTICULAR REPLACEMENT

The follow-up work of the late Drs. William Darrach and Clay Ray Murray during the evolution of the abduction, traction-suspension and pin fixation periods motivated the experiments on articular replacement, because of the shortcomings of the then existing methods. We can cite again the words of Colonna (7), who in 1948 summarized: "From the best statistics available today, one may anticipate the development of late aseptic necrosis in approximately one third of the cases united by bony union." In other words, it would be conservative to say that well over 50 per cent of fractured hips treated with pinning, traction or plaster abduction ended in poor results or death. Hardly anything could have been worse. The author (8) in 1941 presented a study on internal prostheses for injured joints at the New York-Boston-Philadelphia Fracture Day at the Presbyterian Hospital, New York. Moore and Bohlman (9) reported such a case in 1943, but their approach to the problem was different. Despite careful studies (10–13) by the author and associates, the replacement idea was popularized in Europe by Judet *et al.* (14) and by Jaenicher, McBride, Moore, Thomson, Anderson, Peterson and a host of others in America. Some of this "enthusiastic" operating may have been ill advised and, perhaps, uncritical. It was not the intent of Hey Groves (15) who first studied this problem in 1926, nor yet of the author, to initiate such wholesale use of a method not completely tried and certainly not fully developed (16). Perhaps overuse of the method was not without some good; those who have so used it have reported their poor results. May we, with dispassionate optimism, look forward to improvement? This we shall do, despite the fact that some of the harvest of "enthusiastic" operating is already being gathered (17). The following 2 cases, taken from a series, illustrate that:

1. The method of articular replacement holds good promise for mobilizing patients in whom other methods have failed.
2. In certain types of fractures, the surgeon must face the fact that no other method now in use can mobilize the patient, give him a pain-free, functioning hip, and offer reasonable expectancy with respect to both survival and function.

*Case 1.* This case was reported in a previous paper and is reconsidered here as a follow-up study five years and three months after replacement. The patient was injured in April 1946, when she sustained a subcapital fracture of the left femur. It was treated by insertion of a Smith-Peterson nail. About a year and two months after pinning, the pin was removed because of pain. At that time she was a crutch invalid. There was obvious nonunion, with aseptic necrosis of the head, absorption of the neck, and about two inches of shortening (Fig. 1). On February 24, 1948, at the age of 64, almost two years after pinning, she was reoperated on and the necrotic femoral head was removed. An O.N.R.-type (Hudack) replacement was used to restore the length and give her a useful hip (Fig. 2). Because of the restoration, she had persisting gluteal pain for about three months. Matters

FIG. 1. Case 1. Roentgenogram of hip almost two years after injury, and before articular replacement. The pin had already been removed.

were also complicated by the development of an acute gallbladder condition and a thrombophlebitis in the leg which had been operated on. Despite these complications, she was discharged on her thirty-eighth postoperative day, walking with crutches. Her response to inquiry this February, five years after replacement (Fig. 3), was "I think I sort of miss the attention given me. Now I am just another patient. I do very well in the house. I do have a slight limp and, at times, my leg swells some at the end of the day, but I do not have any pain at all—sometimes a tired feeling after walking. For that reason, I am unable to walk far. I still use a cane when I go out. Sometimes I think that it is fear that I might lose my footing. I do not seem to be able to put too much pressure on either foot. I am not overlooking the fact that age enters into it also."

*Case 2.* This 71-year-old white male fell and broke his left hip (Fig. 4) about a year and eight months prior to entry. At that time, the hip was pinned (Fig. 5). His past history was noncontributory, except that he had palpitation on exertion. His system review revealed a nonunion of the left hip, a moderate emphysema and moderate arteriosclerosis. His laboratory data were not particularly unusual, except that the concentration of alkaline

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Case cited through courtesy of Drs. W. H. McGaw, W. F. Kubicek Jr. and J. E. Brown.

FIG. 2

FIG. 3

FIG. 2. Case 1. Post operative roentgenogram following replacement of the aseptic head and part of the neck and trochanter of the femur. Feb. 26, 1948.

FIG. 3. Case 1. Follow-up roentgenogram five years and two months after operation. Observe that the greater trochanter has regenerated in part, and that there is comparatively little migration of the appliance into the femur, at the level of the lesser trochanter. The sclerosis about the mid-shaft is probably because of electrolytic activity in the region of junction between the main stem shank and the perforated prongs. In the early models we were biased by some experience with stainless steel in other applications.

FIG. 4. Case 2. Fracture of the femoral neck. Note the shortening and the pagetoid changes in the pelvis.

phosphatase was 13.7 u/100 cc. (King Armstrong). X-ray examination showed what could be interpreted as Paget's disease of the left pelvis (Fig. 6). On April 3, 1953 he was operated on, using a Smith-Peterson approach. An O.N.R.-type (Hudack) replacement was inserted, which had been made to measurement in order to restore some of the inch of shortening which was present when the pin had been removed and the absorption had stabilized

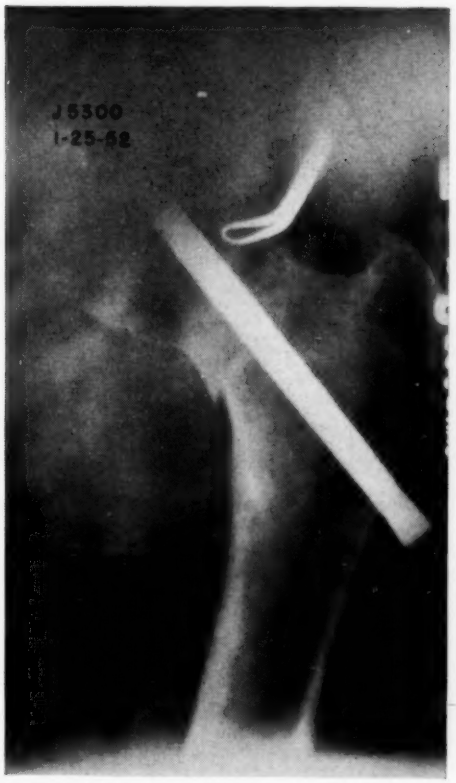


FIG. 5. Case 2. Roentgenogram showing results of pinning operation.

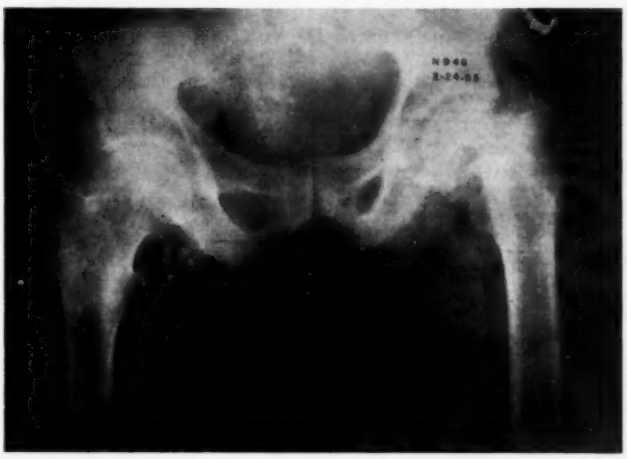

FIG. 6. Case 2. Roentgenogram showing aseptic necrosis of the head of the femur and shortening and absorption of the neck (pin removed).

(Fig. 7). Except for some hypotension just after the operation, his hospital stay was uneventful. On April 21, not quite three weeks after operation, a short-leg hip spica was applied and the patient was gradually mobilized. By May 6 he was walking fairly well with crutches; the leg was able to bear some weight and there was no pain. He went home six weeks after operation, walking with crutches, after having been virtually a bed invalid

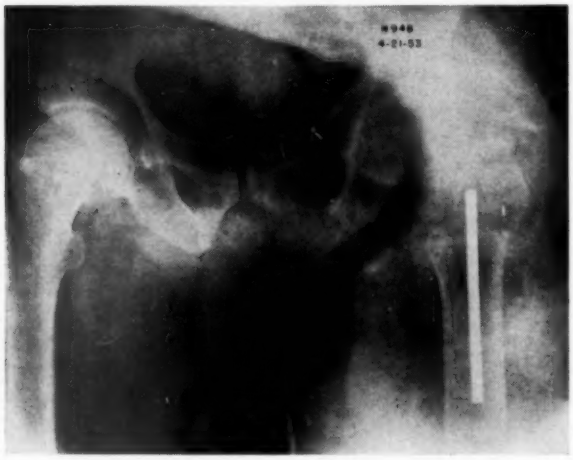

FIG. 7. Case 2. Roentgenogram of hip after the necrotic head of the femur had been replaced.

for two years because of pain, probably more from the fracture than from the Paget's disease.

These 2 cases exemplify a transitional perspective in the treatment of fractured hips. In cases of fracture of the femoral neck with obliquity and displacement which preclude bony union and predicate aseptic necrosis, some institutions may already be using primary replacement and excision of the head. We have not done so, as yet, because we do not feel justified in using premade replacement elements, unless they are to the measure of the patient treated. On the other hand, we have not yet become geared to the refinement of having the elements made to order in a day.

In the consideration of the foregoing 2 patients it must be remembered that both of them had fractured the femoral neck. Both had been treated by skilled surgeons in good hospitals. They had been subjected to two operations before replacement, with the additional risk and the inevitable complications which move in the wake of such procedures. Yet, despite an invalidism of about two years' duration they are now both mobilized. In one patient the follow-up period has now extended over five years. During that time, she has had a normal, relatively pain-free existence. The other patient, mobilized after two years of pain and severe disability, is now at least able to care for himself. When fresh injuries of this type are treated by replacement surgery, the patients are mobilized as quickly as with pinning and possibly more quickly. Moreover, there can be no question of nonunion and aseptic necrosis. When the region which has been deprived of blood supply is replaced by means of the described appliance, needless operations are avoided. In the 2 cases reported here, two years of invalidism also could have been prevented.

The replacement elements are not perfect. We are still trying to improve them, both in design and material. The design has been worked out, after trying many designs clinically. The ideal material for fabrication is not available, but we know

what its physical and biologic characteristics should be. We believe that the replacement element should be measured to the needs of the individual case and tailor-made to fulfill individual requirements.

SUMMARY

We have traced the evolution of restitutive surgery of the hip from the time of Sir Astley Cooper, to the present. Comparison of the prognosis in the case of a fractured hip a hundred years ago, with the present-day status, gives some idea of the progress made. The prognosis one hundred years ago was grim; except in the highly skilled hands of certain surgeons, it was about equally divided between invalidism or death. At the present time, in skilled hands, even in the cases which previously had a poor prognosis, patients may be out of bed in a week, and walking with crutches in three weeks. Within three months they can be leading relatively normal lives.

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# DETACHMENT OF THE RETINA

P. ROBB McDONALD, M.D.*

*University of Pennsylvania School of Medicine, Philadelphia, Pa.*

Retinal detachments were recognized as a cause of blindness long before the development of the ophthalmoscope, although Arlt (1) and Von Graefe (2), in 1853, were the first to publish ophthalmoscopic descriptions of a retinal detachment and de Wecker (3), in 1867, was the first to recognize that a tear or break in the retina might be responsible for the separation. Since that time ophthalmologists have been attempting to cure retinal detachments, although a defeatist attitude was prevalent until Gonin (4), in 1919, presented his thesis of curing the detachment by cauterizing the hole.

The modern era of retinal detachment surgery is, therefore about thirty years old. The present methods of diathermy operation are successful in the majority of the cases. Although statistics may vary with the selection of cases, an overall cure of 70 to 75 per cent of cases is expected by most ophthalmologists who perform any volume of detachment surgery.

The problem is one that should concern every physician and especially those interested in the patient over 50 years of age. In a personal series of nearly 200 patients, 55 per cent were over 50 years old. In an unselected group of 127 patients from the clinics of the Wills Eye Hospital, Purnell (5) found the same percentage. Smith and Pierce (6), in a series of 451 patients from the Retina Service of the Massachusetts Eye and Ear Infirmary, found 56 per cent over 50 years of age. With increasing longevity, this percentage can be expected to increase.

## ETIOLOGY

The etiology of retinal detachment is a complex and rather obscure. Our statistics and those of Duke-Elder (7) show that the maximum incidence is between the ages of 50 and 60, that is, in the decade when senile changes are most likely to begin. The degenerative changes may effect both the vitreous and the retina. Wadsworth (8) and others have shown histologically that contracture of the vitreous can tear a hole in the retina if there is a vitreo-retinal adhesion. Not all tears are caused by vitreous contracture, but it is generally accepted that a break in the continuity of the retina precedes the development of a detachment. Cystic degeneration in the retinal periphery may also lead to detachment. This type of degenerative change is best seen in patients who have had a cataract removed. The inability to see these small peripheral holes may account in some measure for the poorer prognosis in this age group.

Myopia is another factor that must be considered in any discussion of the etiology of retinal detachment. In Smith and Pierce's series, approximately 22 per cent of their patients had a myopia of greater than 3 diopters. As a rule, de-

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* Office address: 1930 Chesnut Street, Philadelphia 3.

tachments develop earlier in life in these patients, especially if they have a high degree of myopia.

The third most important etiologic factor is trauma, either direct or indirect. Although it is hard to evaluate indirect trauma, it is unquestionable that in the age group considered in this discussion the onset of symptoms is frequently related to stumbling, hitting the head, or other relatively benign trauma. In these cases undoubtedly the pathologic changes in the retina and vitreous were already present, but the accident was enough to start a chain of events leading to the detachment. Indirect trauma as a cause of retinal detachment leads to many medico-legal controversies. The incidence of retinal detachments is higher in males than in females, in the ratio of 60 to 40. This can probably be explained by the greater exposure to trauma, direct or indirect, that the male encounters in his everyday activities.

## SYMPTOMS

Most patients are unaware of the nature of their condition and seek advice solely because they have noticed a failure in visual acuity. On questioning, they may state that some time previously they had noticed flashes of light. These are most commonly seen in the lower nasal field. They may have noticed a sudden shower of vitreous opacities or a small defect in their field of vision. The defect may have started as a small wave, which subsequently suddenly obscured their vision. Because the great majority of the holes in the retina are found in the superior temporal quadrant of the eye, the subjective disturbances are usually first noted in the lower visual field. Patients presenting any of these symptoms should be referred to an ophthalmologist. Although flashes of light and a shower of vitreous opacities are not pathognomonic of a retinal detachment, nevertheless in many of these cases, even though a detachment of the retina is not present, careful scrutiny of the peripheral retina with an indirect ophthalmoscope may reveal a small fresh break in the retina. This may be the precursor of a detachment and the patient should be kept under close surveillance.

## DIAGNOSIS

Unfortunately the diagnosis of any retinal detachment is frequently all too easy by the time the patient is first seen by the ophthalmologist. We would prefer seeing patients when the diagnosis would be more difficult, especially before macular vision is lost. The earlier a detachment is recognized and the less extensive it is, the better the prognosis for good vision.

The differential diagnosis of a serous and solid detachment is usually not difficult. Melanomas of the choroid are the most frequent tumors causing a solid detachment. Metastatic lesions are occasionally seen. Besides the ophthalmoscopic differentiation of the two conditions, the use of radioactive phosphorus ($P^{32}$) may be of help in questionable cases.

## TREATMENT

A retinal detachment is one of the few surgical emergencies in the field of ophthalmology. When the patient is told he will be in bed for two to three weeks and

will be partially incapacitated for two to three months, he may rebel or decide that he will try to get along with one eye for the rest of his life. If he should turn to you for advice or moral support, the operation should be advised if the patient has a life expectancy of five years, unless there are other contraindications. Smith and Pierce found bilateral retinal detachments in 27 per cent of their cases. This percentage is essentially the same as in my group. In a series of 200 patients, I have operated on 35 one-eyed patients who had already lost the fellow eye from a retinal detachment. The sooner ophthalmologists and other physicians realize that (excluding the cases due to direct trauma, such as penetrating wounds) a retinal detachment is essentially a bilateral disease, the sooner we shall start saving some of these patients from blindness for the rest of their days.

Once the patient is hospitalized, it is a generally accepted procedure that he be kept in bed for two to three days before operation. During this time both eyes are bandaged or he wears pinhole goggles and the pupil of the affected eye is dilated. If the detachment is inferior, he is usually propped up in bed; if superior and temporal, he is given one pillow and he lies on the side of his body corresponding to the side of the detachment, in order to facilitate settling of the retina. The patient is not kept immobile with sandbags, and movement of the limbus is encouraged. The usual procedure in the past has been to keep the patient in the chosen position for two weeks following operation. However, many surgeons are giving their patients more liberties and are allowing them out of bed at the end of seven days.

The operative procedure need not be discussed at length. I personally prefer the use of pentothal over local anesthesia. In the hands of a good anesthetist it is a relatively safe procedure. The success of the operation depends to a large extent on the finding of all the retinal breaks, closing them with suitably placed diathermy punctures and permitting adequate drainage of subretinal fluid. The entire procedure takes about one hour.

As stated previously, success is obtained in about 70 per cent of the cases. The principal causes of failure are 1) leaving some of the holes unclosed, 2) disturbances in the vitreous, such as a contracture, which pulls the retina off, and 3) excessive diathermy, which causes shrinkage of the retina or creates new holes.

Retinal detachments are an infrequent complication following cataract surgery. When they do occur they present a serious problem, because in many instances they are associated with gross changes in the vitreous. The prognosis for reattachment in an aphakic patient is about 20 per cent lower than in a phakic patient. Unfortunately, in the absence of a history of direct trauma, if a patient gets a detachment in one eye following removal of a cataract, he stands a very good chance of having the same sequence of events following cataract extraction in the other eye. If a retinal detachment develops in a patient with an immature cataract, every attempt should be made to cure the detachment before attempting to extract the lens. Prior extraction of the lens will lead to a total detachment.

Ophthalmologists have revived an old and previously discarded operation for those patients in whom the classic diathermy operation does not seem to be successful. The operation consists of excising a piece of sclera about 30 mm. long and

3 to 4 mm. wide along half of the eyeball. The anterior edge of the scleral resection is usually 10 to 12 mm. from the limbus. One may resect the entire thickness of sclera or leave a thin sheet overlying the choroid; this is then buckled into the eye when the scleral edges are approximated with sutures. The operation is indicated in patients in whom the retina does not settle during bed rest, or in those who have markedly degenerated retinas with numerous scattered holes. The principle of the operation is that, if the retina cannot be brought back to the choroid and sclera, the outer coats should be advanced to the retina. It permits one to obtain a large area of choroidal retinal adhesions with minimal damage to the retina and vitreous. It is now being used as a primary procedure in patients known to have a poor prognosis. As more experience is gained and the indications are more clearly defined, one can expect an even greater percentage of cures with retinal detachment surgery.

### PROGNOSIS

The prognosis varies as to the type of detachment, number and size of the holes, condition of the vitreous, the visibility of the fundus and the extent of the detachment. Sometimes even the most favorable cases do progress favorably, whereas at other times a spectacular result may be obtained in an almost hopeless case.

### COMMENTS

The incidence of retinal detachments in the general population is not known. However, all statistics show that over 50 per cent of the cases occur in persons over 50 years of age. With the increasing longevity of the population one can therefore expect an increase in the incidence of retinal detachments. In young individuals most retinal detachments are caused by direct trauma, perforating injuries or a high degree of myopia. In patients over 50 there is the highest incidence of so-called idiopathic detachments. Examination of such patients reveals degenerative changes in the vitreous and retina. These are sometimes associated with myopia or cataract, though in many instances the eyes are essentially normal, save for peripheral degenerative changes in the retina. Inasmuch as direct trauma is unforeseen, there is little advice we can give with respect to prevention. Anyone who has had a detachment in one eye should avoid sports that may cause jars or falls, *i.e.*, horseback riding and diving. There are no known drugs that will strengthen the retina or prevent degenerative changes in the vitreous.

A patient who complains of flashes of light, a sudden shower of vitreous opacities, a defect in his field of vision or a wavy curtain in front of his eye should be suspected of having a retinal detachment and be referred to an ophthalmologist for evaluation. If a retinal detachment is present the patient should be encouraged to have it operated upon, because there is a better than a 25 per cent chance that eventually a detachment will develop in the fellow eye. The patient need not be immobilized, though complete bed rest for ten to fourteen days is desirable. General supportive measures, such as massage and exercise of the limbs is to be encouraged. Should elderly patients become confused with both eyes bandaged,

pinhole goggles may be used, both before and after operation. The operation is performed more easily and quickly under general anesthesia, though local anesthesia may be used if necessary. With the increased longevity of the population, one may expect an increase in the incidence of retinal detachments. It is very important to make the diagnosis early, since the prognosis is definitely related to the extent and duration of the detachment.

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# AMERICAN GERIATRICS SOCIETY

## THE 1954 ANNUAL MEETING

The 11th Annual Meeting of the American Geriatrics Society will be held at the Hotel Fairmont in San Francisco just preceding the meeting of the American Medical Association. The scientific sessions of the meeting will begin Thursday afternoon, June 17 and continue through Saturday morning, June 19.

Fellows who wish to present a paper at the meeting should send six copies of a title and an abstract not to exceed 300 words to the Secretary, Dr. Malford W. Thewlis, 25 Mechanic Street, Wakefield, Rhode Island, **not later than FEBRUARY 1, 1954.**

## THIRD INTERNATIONAL GERONTOLOGICAL CONGRESS—LONDON

The Third International Gerontological Congress will be held in London, England, *July 19–23, 1954*, under the presidency of Dr. J. H. Sheldon. Arrangements by the British Organizing Committee are well advanced. Dr. R. E. Tunbridge, B.M.A. House, Tavistock Square, London W.C.1, is Chairman of the Committee. An *American Committee* is cooperating with the British Committee, especially in regard to the program. Of this Committee *Dr. W. B. Kountz, 660 S. Kingshighway Blvd., St. Louis 10, Mo., is the Chairman.* The Congress will be both instructive and enjoyable. It is imperative for those planning to attend and to present their work, to send titles of papers, together with abstracts of not more than 250 words, to Dr. Kountz. As in the case of other International Congresses, personal invitations to present papers are not necessary but in the event that these would be helpful in obtaining subsidies for travel, the American Committee will be happy to request the British Organizing Committee to send official invitations.

The Research Committee on Biology and Medicine will meet at the same time as the Third International Gerontological Congress. The Chairman of this Committee is Dr. W. O. Thompson, Chicago, Illinois.

Because the time is short and it is difficult to get transatlantic reservations, except the more expensive ones, blocks of reservations are being held by Convoys Travel Service, 1133 Broadway, New York 10, N. Y. All correspondence concerning *travel information* should be addressed to *Mrs. V. Kelly, 660 S. Kingshighway, St. Louis 10, Mo.*

## BOBST PHARMACAL CO. AWARD IN GERONTOLOGY

The Bobst Pharmacal Co. has paid to the International Gerontological Association, the sum of $1000 to be used as an award for outstanding work in gerontology, having in mind activities in this field throughout the world. The award will be made at the Third International Gerontological Congress in *London, July 19–23, 1954*. Members of the governing body of the International Association will make recommendations to the officers of this Association and they will select a candidate for the award from among these recommendations.

Following the Second International Gerontological Congress in St. Louis in 1951, the Bobst Pharmacal Co. made two awards on recommendation of the officers of the Congress. One was to Dr. Albert I. Lansing of the Department of Anatomy, Washington University School of Medicine, St. Louis, for his paper entitled "A Cytoplasmic Factor in Ageing" and the other to Dr. J. A. Huet, Hospital de Nanterre, Paris, for his paper entitled "Organization et Rentabilité d'un 'Senat' dans une Usine Française de Fabrication d'Automobiles." Each of these awards was in the amount of $250.

## SPANISH CONFERENCE ON GERONTOLOGY

The Sociedad Espanola de Gerontologia will hold a Conference in Valencia, Spain, *July 1–3, 1954*, under the presidency of Dr. M. Beltran-Baguena. It is

expected that the program will be a very attractive one and will bring together many contributions from Spain and the Latin American countries. Moreover, the location of this meeting is very enticing. The time for holding it was decided upon in conference with the International Association of Gerontology. It will be convenient for those attending the International Congress on Gerontology in London, July 19–23, 1954, to go to the Valencia Conference beforehand. For details regarding hotels and other matters, write directly, airmail, to Dr. M. Beltran-Baguena, Paz 44, Valencia, Spain.

## BOOKS RECEIVED

*American Lecture Series*. Charles C Thomas, Publisher, Springfield, Illinois.

*Inhalation Therapy and Resuscitation*. By MEYER SAKLAD, M.D., Director, Department of Anesthesiology, Rhode Island Hospital, Providence, R. I. A monograph in the Bannerstone Division of American Lectures in Anesthesia, edited by JOHN ADRIANI, M.D.; 338 pages; 130 illustrations. 1953.

*Psychosomatic Approach to Gynecology and Obstetrics*. By FRITZ WENGRAF, M.D., Adjunct Neuropsychiatrist, Beth Israel Hospital, New York, N. Y. A monograph in the Bannerstone Division of American Lectures in Gynecology and Obstetrics, edited by E. C. HAMBLEN, M.D.; 365 pages; extensive bibliography; 1953.

*Shame and Guilt: A Psychoanalytic and a Cultural Study*. By GERHART PIERS, M.D., Institute for Psychoanalysis, Chicago, Illinois, and MILTON B. SINGER, PH.D., Professor of the Social Sciences, The College of the University of Chicago. A monograph in American Lectures in Psychiatry, edited by ROY R. GRINKER, M.D.; 96 pages; 1953.

*The Allergic Patient and His World*. By FLORENCE EASTTY SAMMIS, M.D., Assistant Attending Physician in Allergy, Nassau Hospital, Mineola, N. Y., and OREN C. DURHAM, Chief Botanist, Abbott Laboratories, North Chicago, Ill. A monograph in the Bannerstone Division of American Lectures in Allergy, edited by MAX SAMTER, M.D.; 166 pages; 12 illustrations, 1953.

*Enzymatic Concept of Anaphylaxis and Allergy, and the Role of Eosinophils in Anaphylactic Reactions Related to Hormonal Alterations*. By Z. Z. GODLOWSKI, M.D., PH.D., Research Fellow of the Carnegie Trust; Acting Professor of Physio-pathology and Lecturer in Clinical Medicine at the late Polish School of Medicine, Edinburgh University, Scotland, with a foreword by A. MURRAY DRENNAN, M.D., Professor of Pathology, University of Edinburgh; 128 pages; 17 illustrations—many in color; 1953. Edinburgh and London, E. & S. Livingstone Ltd. Baltimore, Md., The Williams & Wilkins Co. Price $3.50.

*Training and Research in State Mental Health Programs*. A Report to the Governors' Conference; 380 pages with tables, charts and index. Published in July 1953 by the Council of State Governments, 1313 East Sixtieth Street, Chicago 37, Illinois. Price $5.00.